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VOICE DISORDERS AND TREATMENT EFFECTS IN PARKINSON'S DISEASE STUDIED WITH A PORTABLE VOICE ACCUMULATOR

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Karolinska Institutet

Stockholm 2020

Published by Karolinska Institutet.
Printed by Exakta.

ISBN 978-91-7831-725-7

Department of Clinical Science, Intervention and Technology
Division of Speech and Language Pathology

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THESIS FOR DOCTORAL DEGREE (Ph.D.)

which, by due permission from Karolinska Institutet, will be publicly defended in lecture hall Månen, Alfred Nobels Allé 8, Karolinska Institutet, Campus Flemingsberg

Friday March 6th, 2020 at 9 AM

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To my family. To Greta and Brita, I love you and I like you.

“All things are so uncertain, and that's exactly what makes me feel reassured”

- Too-Ticky

ABSTRACT

Background: Information about voice use outside the clinical setting has traditionally consisted of subjective data collected via interviews or questionnaires. Quantitative, objective information about voice use in daily life could increase our understanding of the challenges faced by patients outside the controlled clinical environment. There is a high prevalence of hypophonia in individuals with Parkinson's disease (PD). Objective information regarding voice use would be of value, not the least for this population considering the changes in perception of speech production and cognition found in PD, and may be collected with the use of a portable voice accumulator

Objectives: The aim of this thesis was to study voice use and communication in daily life in individuals with PD and healthy matched controls using a portable voice accumulator. A further aim was to assess the outcome following biofeedback intervention provided with a portable voice accumulator with the goal to increase voice sound level in daily life for individuals with hypophonia related to PD.

Materials and methods: In **study I**, the portable voice accumulator VoxLog was used to monitor voice use in daily life regarding voice sound level and phonation ratio in different levels of environmental noise for twenty-one individuals with PD and twenty-one matched healthy controls during a week-long registration period. In **study II**, treatment outcome following Lee Silverman Voice Treatment (LSVT LOUD®) was assessed in a pseudo-single case study through monitoring of voice use in daily life before, during, and after treatment as well as at follow-up one year after treatment. In **study III**, the portable voice accumulator VoxLog's biofeedback function was used to provide biofeedback intervention during one week for six individuals with PD with the goal to increase voice sound level in daily life. **Study IV** focused on experimentally testing the biofeedback function of the VoxLog to assess how different feedback frequencies can be achieved by adjusting the available settings. Six different biofeedback settings were assessed during semi-structured conversations with twenty participants. In **study V**, a four-week long biofeedback intervention period was evaluated for eight individuals with PD. Voice use was monitored the week before intervention, during the four-week intervention period, the week after intervention and one week at follow-up, three months post intervention.

Results: Seventy-eight participants were included in the analysis and field registrations were performed for a total of 127 weeks in the project. The week-long registrations of voice use in **study I** showed that individuals with PD use their voice 50-60% less than their matched healthy controls. The difference increased in situations with loud environmental noise, which in many cases are social situations. A difference in mean voice sound level was found where individuals with PD used a voice sound level 6-8 dB lower than their matched healthy controls. Voice sound level used in daily life differed significantly from the voice sound level during controlled studio registrations for both the male and female groups. **Study II** showed that the changes in voice sound level after LSVT LOUD® when studied in daily life with a portable voice accumulator reflect earlier reported changes registered during controlled studio

recordings. In **study III**, a significant increase in voice sound level in relation to the environmental noise was found during the intervention week but the effect did not remain when the biofeedback was removed. Based on the findings in **study IV**, a systematic procedure to configure the biofeedback settings in the VoxLog was recommended to achieve a low feedback frequency, known to facilitate retention after training in the motor learning literature. The results from **study V** showed an increase in voice sound level in relation to the environmental noise following a four-week long biofeedback intervention and the effect was still present at the three-month follow-up. Results from screening with the Montreal Cognitive Assessment showed that individuals who scored above the cut-off for mild cognitive impairment had more positive and lasting outcomes compared to the group who scored below the cut-off for mild cognitive impairment.

Conclusions: Objective assessment of voice use in daily situations outside a controlled clinical setting is a valuable complement to traditional methods and can increase the ecological validity of our assessments. Providing biofeedback to help individuals with hypophonia secondary to PD increase their voice sound level may be an alternative or complement to voice therapy performed at a clinic. Further research with more participants is however needed to determine the efficacy of this intervention approach, and development of the biofeedback capabilities of portable voice accumulators are needed to improve the method.

SAMMANFATTNING

Bakgrund: Information om röstanvändning utanför kliniken inhämtas traditionellt från intervjuer eller frågeformulär. Objektiv och kvantifierbar information om röstanvändning i vardagen skulle kunna öka kunskapen om de utmaningar som patienter med röststörningar möter utan för den kontrollerade klinikmiljön. Det är mycket vanligt att röststyrkan blir nedsatt hos personer med Parkinsons sjukdom. Objektiv information om röstanvändning kan inhämtas med hjälp av bärbara röstackumulatorer och skulle vara av stor nytta för patientgruppen då förändringar i hur den egna rösten uppfattas och kognitiv svikt är vanligt relaterat till sjukdomen.

Syfte: Målet med denna avhandling var att studera hur röstanvändning och kommunikation påverkas i vardagen för personer med Parkinsons sjukdom jämfört med matchade röstfriska kontrollpersoner med hjälp av en bärbar röstackumulator. Ett ytterligare mål var att utvärdera effekten av en intervention där individer med Parkinsons sjukdom får kontinuerlig återkoppling i vardagen gällande talets röststyrka med målet att hjälpa dem höja röststyrkan.

Material och metoder: Sammanlagt sjuttioåtta deltagare ingår i analysen och materialet omfattar totalt 127 veckor av långtidsregistrering av röstanvändning i vardagen. I **studie I** användes röstackumulatorn VoxLog för att registrera röstanvändning i vardagen avseende röststyrka och fonationstid under en vecka för tjugotvå deltagare med Parkinsons sjukdom och tjugotvå matchade, röstfriska kontrollpersoner. I **studie II** utvärderades effekten av Lee Silverman Voice Treatment i en fallstudie där röstanvändning registrerades med röstackumulator före, under och efter behandling samt vid uppföljning upp till ett år efter att behandlingen avslutats. I **studie III** användes röstackumulatorn VoxLogs återkopplingsfunktion i träningssyfte där sex personer med Parkinsons sjukdom fick kontinuerlig återkoppling avseende röststyrka under en veckas tid med målsättningen att höja röststyrkan i vardagen. **Studie IV** fokuserade på att experimentellt utvärdera de återkopplingsinställningar som går att justera i mjukvaran för att uppnå en önskad återkopplingsfrekvens. Sex olika återkopplingsinställningar testades under semistrukturerade konversationer med tjugo deltagare. I **studie V** utvärderades en fyra veckor lång återkopplingsperiod för åtta individer med Parkinsons sjukdom. Röstanvändning registrerades veckan före intervention, under de fyra veckorna då återkoppling gavs, en vecka efter intervention samt en vecka vid uppföljning tre månader efter interventionsperioden.

Resultat: Resultaten från den veckolånga registreringen av röstanvändningen i **studie I** visade att deltagarna med Parkinsons sjukdom använder sin röst 50 - 60 % mindre än matchade röstfriska kontrollpersoner. Skillnaden ökade i miljöer med högt bakgrundsbuller, vilket i många fall är sociala situationer. En skillnad i genomsnittlig röststyrka sågs där personer med Parkinsons sjukdom använde en röststyrka som var 6 - 8 dB lägre än den röstfriska kontrollgruppen. Röststyrkan som användes i vardagen skiljde sig signifikant från röststyrkan som användes under kontrollerade registreringar i studiomiljö för alla grupperna.

I **studie II** visades en ökad röststyrka under röstanvändning i vardagen efter Lee Silverman Voice Treatment som motsvarade tidigare rapporter baserade på kontrollerade inspelningar i studiomiljö. I **studie III** fann man en ökad röststyrka i relation till omgivande buller under interventionsveckan men effekten kvarstod inte när återkopplingen inte längre administrerades. Utifrån resultaten i **studie IV** rekommenderas en systematisk process för att välja återkopplingsinställningar när man använder VoxLog för att uppnå en låg återkopplingsfrekvens vilket främjar en bestående inlärning enligt tidigare forskning om motorisk inlärning. Resultaten från **studie V** visade en ökad röststyrka i relation till bakgrundsbuller under röstanvändning i vardagen efter fyra veckors intervention med återkoppling avseende röststyrka. Effekten var kvarstående vid uppföljning efter tre månader. Testning med screeningmaterialet Montreal Cognitive Assessment visade att deltagare som presterade över gränsvärden för mild kognitiv svikt uppnådde bättre och mer bestående resultat efter interventionen än deltagare som presterade under gränsvärdena för mild kognitiv svikt.

Slutsatser: Objektiv bedömning av röstanvändning i vardagen utanför en kontrollerad miljö är ett värdefullt komplement till traditionella metoder och kan öka den ekologiska validiteten av röstanalyser. Möjligheten att ge kontinuerlig återkoppling på röststyrka i vardagen för personer med Parkinsons sjukdom för att hjälpa dem höja sin röststyrka kan vara ett effektivt alternativ eller komplement till traditionell röstbehandling. Fortsatt forskning med flera deltagare krävs dock för att säkert fastställa nyttan av metoden. Utvecklande av återkopplingsfunktionen i framtidens bärbara röstackumulatorer skulle även stärka metoden.

LIST OF SCIENTIFIC PAPERS

I. **Körner Gustafsson, J**., Södersten, M., Ternström, S., & Schalling, E. Voice use in daily life studied with a portable voice accumulator in individuals with Parkinson's disease and matched healthy controls. Journal of Speech Language and Hearing Research. 2019; 62(12): 4324-4334.

II. **Körner Gustafsson, J.**, Södersten, M., Ternström, S., & Schalling, E. Long-term effects of Lee Silverman Voice Treatment on daily voice use in Parkinson's disease as measured with a portable voice accumulator. Logopedics Phoniatrics Vocology. 2018; 44(3):124-133.

III. Schalling, S., **Gustafsson, J.**, Ternström, S., Bulukin-Wilén, F., & Södersten, M. Effects of tactile biofeedback by a portable voice accumulator on voice sound level in speakers with Parkinson's disease. Journal of Voice. 2013; 27(6):729-737.

IV. **Gustafsson, J.**, Södersten, M., Ternström, S., & Schalling, E. Motor-learning-based adjustment of ambulatory biofeedback on vocal loudness for patients with Parkinson's disease. Journal of Voice. 2016; 30(4):407- 415.

V. **Körner Gustafsson, J.**, Södersten, M., Ternström, S., & Schalling, E. Treatment of hypophonia in Parkinson's disease through continuous biofeedback in daily life using a portable voice accumulator. Manuscript.

CONTENTS

LIST OF ABBREVIATIONS

APM	Ambulatory Phonation Monitor
cZi	Caudal Zona Incerta
dB	Decibel
DBS	Deep Brain Stimulation
$Diff_{voice/noise}$	Difference in voice sound level and noise sound level
GPi	Globus Pallidus Interna
Hz	Hertz
LSVT	Lee Silverman Voice Treatment
MCI	Mild Cognitive Impairment
MoCA	Montreal Cognitive Assessment
PD	Parkinson's Disease
PVA	Portable Voice Accumulator
QASD	Questionnaire on Acquired Speech Disorders
SLP	Speech Language Pathologist
SOR	Self-to-Other Ratio
STN	Subthalamicus Nucleus
VHI	Voice Handicap Index

1 INTRODUCTION

Being able to participate in social interaction and communicate freely is one of the most important aspects of our daily life. Eadie and colleagues (2006) define communicative participation as taking part in life situations where knowledge, information, ideas or feelings are exchanged. For many, the ability to communicate is taken for granted until one finds itself in a situation where we are not able to do so effectively. Problems with communication can be, for example, the frustration caused by a distorted message due to bad phone connection or losing your voice due to a cold. In most cases, the communication breakdowns are transient, a problem easily overcome. The problems can however also be more severe, and in some cases permanent. Communication difficulties can also originate from an impairment related to a disease or be of a developmental nature, often described as a communication disorder.

The American Speech-Language-Hearing Association (1993) defines a communication disorder as "an impairment in the ability to receive, send, process and comprehend concepts or verbal, nonverbal and graphic symbol systems. A communication disorder may be evident in the processes of hearing, language and/or speech. A communication disorder may range in severity from mild to profound. It may be developmental or acquired. Individuals may demonstrate one or any combination of the three aspects of communication disorders. A communication disorder may result in a primary disability or it may be secondary to other disabilities". A communication disorder can, as one might imagine, present itself in many ways. Communication disorders secondary to neurological disease is one common example.

1.1 PARKINSON'S DISEASE

1.1.1 Etiology and symptoms

Parkinson's disease (PD) is a neurodegenerative disease resulting from a loss of dopaminergic neurons in the brain, mainly the basal ganglia, which in turn leads to a dopamine deficiency. It is one of the most common neurological disorders and the fastest growing in terms of increasing prevalence globally (GBD 2016 Parkinson's Disease Collaborators, 2018; Rossi et al 2018). The neuromuscular deficits following the dopamine loss in the brain result in a restriction of range and speed of movements, leading to a variety of motor symptoms. The main gross motor symptoms include rest tremor, rigidity, bradykinesia and postural instability. Speech and voice are also commonly affected in PD. Hypokinetic dysarthria is the subtype of dysarthria associated with PD, and can occur as one of the first symptoms, but may also present itself several years after PD onset (Duffy, 2013). In autopsy-confirmed cases of PD, approximately 90% showed signs of dysarthria during the disease progression (Müller et al., 2001).

The most common symptom of hypokinetic dysarthria is reduced voice intensity. Fox and Ramig (1997) performed a comparison of voice intensity during various speech tasks in a controlled environment between individuals with PD and healthy controls. For the PD group, they found a voice intensity that was 2-4 dB lower, which the authors equated to a 40% reduction in vocal loudness. Other symptoms include imprecise articulation, monopitch and intensity, breathiness, hoarseness and variable speech rate (Duffy, 2013). Cognitive and psychiatric symptoms are also common in PD, including dementia, depression, disturbed sleep patterns and hallucinations (Duffy, 2013). Speech motor deficits impacting intelligibility, combined with cognitive and psychiatric changes, can lead to major limitations in communicative participation and social interactions (Miller et al., 2006; Hartelius et al., 2008; Baylor et al., 2011; Schalling et al., 2017; Yorkston et al., 2017).

Miller et al. (2006) performed in-depth interviews with 37 men and women with PD about how communication had been changed as a result of their disease. Their main concern was not how their speech and voice had been altered, but rather how these changes affected their concept of self and their ability to participate in social situations. Social withdrawal was a recurring example, in some cases from being shut out of conversations as a result of an inability to keep up with the other speakers; and also as a coping strategy to preserve strength and make sure that they would be able to say something if it really mattered.

1.1.2 Pharmacological treatment

There are no curative treatment options for PD, but there are several options available to alleviate motor symptoms. Pharmacological treatment mainly focuses on increasing the dopamine levels in the brain and generally produce good results regarding gross motor function, especially during earlier stages of the disease progression. Over time, side-effects such as dyskinesias are common. Maintaining a consistent medication response is a challenge for many as the disease progresses, and on-off effects are common. This can result in symptom fluctuations during the beginning, peak or end of a dosage cycle. Furthermore, the effects on dysarthria are limited and variable. Some studies have shown a positive effect of pharmacological intervention on specific speech and voice parameters (De Letter, Santens, de Bodt et al., 2007; De Letter, Santens, Estercam et al., 2007; Ho et al., 2008; Skodda, 2010) whereas other studies have shown no improvement, particularly regarding changes in voice sound level (Ramig et al., 2007; Plowman-Prine et al., 2009; Pinho et al., 2019).

1.1.3 Surgical treatment

Surgical treatment options such as Deep Brain Stimulation (DBS) have become increasingly common during the last decade. Electrodes are surgically implanted to continuously stimulate specific targets in the brain. DBS is not a standard treatment option

but is often considered in advanced stages of the disease, when pharmacological treatment is less effective and more difficult to manage (Breit et al., 2004). The effect of DBS varies depending on the locus being stimulated and how the electrical stimulation is administered. Common targets include the subthalamicus nucleus (STN DBS) (Benabid, 2003), globus pallidus pars interna (GPi DBS) (Rodriguez-Oroz et al., 2005) and the caudal zona incerta (cZi DBS) (Plaha et al., 2006). The impact on speech varies, and may even be negative (Pinto et al., 2005; D'Alatri et al., 2008; Klosterman et al., 2008; Karlsson et al., 2011; Karlsson et al., 2012; Schulz et al., 2012; Karlsson et al., 2013; Karlsson et al., 2014; Sandström et al., 2016).

1.1.4 Speech and voice treatment

Behavioral treatment approaches provided by speech and language pathologists (SLPs) are the leading treatment options for speech and voice symptoms today, as pharmacological and surgical treatments have a limited and variable effect (Atkinson-Clement et al., 2015). The historical view that speech changes in PD may be resistant to behavioral intervention (Weiner & Singer, 1989) has changed over the last decades, as several studies have shown positive and lasting changes after behavioral intervention (Ramig et al., 2001; Sapir et al., 2011; Fox et al., 2012; Atkinson-Clement et al., 2015; Watts, 2016; Ramig et al., 2018). The treatment option with the strongest evidence today is the Lee Silverman Voice Treatment (LSVT LOUD®), with reported positive outcomes regarding increased voice intensity for up to two years after treatment (Ramig et al., 2001; Sapir et al., 2011; Fox et al., 2012; Ramig et al., 2018). It is an intensive treatment program, focusing on increasing effort to increase voice intensity. The treatment program consists of sixteen individual hour-long treatment sessions administered over four weeks. In addition, daily exercises are performed by the patient at home. The exercise program includes tasks such as maximum sustained phonation and production of functional phrases with a loud voice, and hierarchically structured speaking exercises aimed at rescaling subjectively needed effort to produce adequate intensity during speech.

Despite the positive changes during clinical follow-up assessment after intensive voice treatment, there are still many patients that struggle with the carryover of treatment effect to their habitual speech outside the clinical setting. This might be explained by the changes in sensory perception reported for individuals with PD, which could lead to an underestimation of required effort when speaking (Ho et al., 2000). A possibly impaired ability to regulate and scale intensity and range of motor functions in PD could also be a contributing factor (Klockgether et al., 1995; Demirci et al., 1997). Deficits in internal cueing have also been suggested as a factor, which could create difficulties adjusting voice intensity in response to implicit cues, whereas external cues used during treatment still can be used efficiently (Ramig et al., 2007). A way to facilitate a more successful carryover of treatment effects could be to provide continuous biofeedback on voice use in daily life.

1.2 TRADITIONAL METHODS TO RECORD SPEECH

Assessment and analysis of speech and voice function is traditionally based on standardized clinical assessment tools and audio recordings made in controlled environments. Speech tasks used during controlled recordings typically include spontaneous speech, reading of words, sentences and text, as well as more specific tasks such as sustained phonation, which can be used for both perceptual assessment and acoustic analysis (Duffy, 2013). The motivation for making standardized recordings in a controlled environment is to ensure a reliable and replicable assessment, which is important both for research purposes and for clinical work, e g for comparson of function before and after treatment. Voice use during such controlled tasks and settings might however differ greatly from voice use during habitual speech in daily life. In such uncontrolled and varying settings there are many factors that can affect the speaker, and the requirements and challenges imposed on the voice increase. Environmental noise, stress, physical movement, emotional state as well as the cognitive load of participating in a conversation, which increases with topic complexity, introduce challenges that are not comparable to the situation during controlled recordings. Patients' subjective descriptions through interviews or standardized self-report questionnaires are often used to include assessment of factors affecting the voice, but reports of subjective experiences of voice use are not necessarily reliable. A more ecologically valid approach to assessment of speech and voice could be to study voice use outside a clinical setting objectively, using wearable devices with the ability to register important speech and voice parameters (Mehta et al., 2015).

1.3 AMBULATORY MONITORING OF VOICE USE

1.3.1 Methods for monitoring of voice use outside a clinical setting

Wearable devices with the ability to monitor health parameters have been popularized and made available to the general public in recent years, for instance in the form of smartwatches. Such technical aids could be a revolutionary addition to speech and voice assessment, as they can allow for real-time monitoring of voice use in daily life settings. Methods to monitor voice use in daily life have been used in research for several decades, see Szabo Portela (2017) for a review. The clinical availability of such methods has however been very limited. There have been three such devices commercially available to clinicians in different iterations, commonly referred to as portable voice accumulators (PVAs) (Van Stan et al., 2014): the VoxLog (Sonvox AB, Umeå, Sweden), the Ambulatory Phonation Monitor (KayPentax, NJ, USA) and the Vocalog (Griffin Laboratories, CA, USA). There have also been recent ongoing attempts to develop wearable devices to monitor voice and speech function, currently in a research phase at the time of writing, including a low-cost device based on existing hardware (Hunter, 2013), a smartphone-based device (Mehta et al., 2015), a smartwatch-based device (Mahler et al., 2016) and a standalone accelerometer-based device (Astolfi, 2016a; Astolfi, 2016b).

The VoxLog, Ambulatory Phonation Monitor and Vocalog are in many ways similar in methodological approaches and functions, but they differ in a couple of key aspects (Wirebrand, 2012). All devices consist of a neck-mounted sensor that is connected to a wearable device, where data is processed, stored and later uploaded to a computer for analysis in the accompanying software. The Ambulatory Phonation Monitor uses an accelerometer to detect the vocal fold vibrations during phonation. It can register fundamental phonation frequency (Hz), time spent phonating (%) and, through a calibration procedure that needs to be repeated before each monitoring session or when the sensor is displaced, it can estimate voice intensity (dB SPL). The Vocalog uses a similar accelerometer method to estimate voice sound level (dB) and to register time spent phonating. The VoxLog uses a combined approach with an accelerometer and a microphone. The accelerometer is used to register fundamental phonation frequency (Hz) and time spent phonating. When the accelerometer detects phonation, the sound pressure level that the microphone transduces is registered as the wearer's voice intensity (dB). When no phonation is detected by the microphone, the input level is registered as the level of environmental noise (dB). No calibration is needed for the VoxLog, as it registers voice intensity and level of environmental noise at the actual distance from the microphone to the source. Together with van Stan and colleagues (2014), a comparison study of these devices has been published which focuses on how their differences in function could impact choice of method used in clinical work; see table 1 below for important differences. All these devices register different aspects of voice function, but do not record the speech signal, which protects the integrity of the wearers and their conversational partners.

Table 1 Description of the characteristics for each of the three commercially available devices (van Stan et al., 2014).

Variables	**APM**	**VoxLog**	**Vocalog**
Voice sound level (dB)	×	×	×
Biofeedback (voice sound level, dB)	×	×	×
Fundamental frequency (Hz)	×	×	
Biofeedback fundamental frequency (Hz)	×	×	
Percent phonation (%)	×	×	×
Environmental noise (dB)		×	
Need for dB SPL Calibration	Daily	None	Once
Max registration duration*	18 hours	7 days	3 weeks

* Maximum registration duration before data needs to be exported to a computer before further registration is possible.

All three commercially available PVAs described above can provide direct biofeedback regarding the wearer's voice intensity. The VoxLog and the Ambulatory Phonation Monitor can also provide biofeedback regarding fundamental frequency. The biofeedback can be delivered in the form of a vibration from the device, worn in the belt or in a pocket, when the speaker goes above or below an adjustable threshold level. In the case of patients with PD, the biofeedback function may be used as a therapeutic device to remind the patient with PD to increase his or her voice intensity in their daily life.

1.3.2 Applications in Parkinson's disease

Individuals with PD commonly report that they feel they have become more withdrawn in social situations as a result of their disease (Miller et al., 2006; Schalling et al., 2017). Monitoring phonation time during habitual speech in daily life could make a valuable contribution to the understanding of the impact of PD on communicative participation. The ability to register voice intensity without calibration and the ability to register level of environmental noise makes the VoxLog the ideal PVA to use when the goal is to monitor voice use in patients with PD, as a decreased voice intensity is one of the major voice symptoms and an increased voice intensity is often the main goal of intervention. Environmental noise is known to impact voice intensity: speakers have been shown to habitually increase their voice intensity in increasing levels of environmental noise. This is commonly referred to as the Lombard effect or the Lombard sign (Lombard, 1911). It is therefore important to be able to control for variations in environmental noise when, for example, evaluating treatment outcome focusing on increased voice intensity with a PVA.

The Lombard effect and how a speaker habitually changes voice intensity depending on environmental noise and speech task have been studied extensively historically (Gardner, 1964; Gardner, 1966; Hanley & Steer, 1949; Korn, 1954; Pickett, 1958; Webster & Klumpp, 1962). Lane and Tranel (1971) described in a review that a speaker generally increases his/her voice intensity in relation to increasing environmental noise as a function of 0.5, with some variation depending on task and setting. Speech in a setting where the environmental noise increases with 6 dBA would generally lead to an increased voice intensity of 3 dB SPL.

The guidelines for speech in noise presented by the Swedish Work Environment Authority describe that a speaker will start to increase the voice intensity when the level of environmental noise starts to go above 40 dBA. A normal voice intensity is still intelligible at a distance of 1 meter when the level of environmental noise is 55 dBA. A loud voice is needed to be intelligible at a distance of 1 meter when the level of environmental noise reaches 70 dBA and a speaker needs to shout or scream to be intelligible in a level of environmental noise of 85 dBA (Arlinger, 1999).

There have been several studies that have looked at how variations in environmental noise affect speech regulation, in individuals with PD in particular (Adams & Lang, 1992; Ho et

al., 1999; Dromey et al., 2000; Sadagopan & Huber, 2007; Stathopoulos et al., 2014). On a group level, individuals with PD have been shown generally to react to increased levels of environmental noise in a way similar to healthy speakers. There are however exceptions within the groups where individuals with PD fail to regulate voice intensity in response to variations in the levels of environmental noise (Sadagopan & Huber, 2007; Stathopoulos et al., 2014). The variability may be a result of individual differences in the ability to regulate intensity, be it related to skill or severity of dysarthria. It could also be due to the fact that the levels of environmental noise imposed on the speaker differed between some studies.

1.3.3 Biofeedback in speech and voice intervention

It is common practice to deliver feedback on performance during behavioral speech and voice treatment using verbal cues or by prompting patients to react to kinesthetic or auditory internal cues. Other approaches, such as delivering feedback through external technical aids to enhance learning during voice intervention have also been used. These include a variety of methods such as visual biofeedback (Scott & Caird, 1983; Laukkanen Syrjä, Latala & Leino, 2004; Norrlinder & Olsson, 2009; Schneider-Stickler, Knell, Aichstill & Jocher, 2012; Kearney et al., 2018), auditory biofeedback (Sadagopan & Huber, 2007), combined auditory and visual biofeedback (Le Dorze, Dionne, Ryalls, Julien & Oullet, 1992) as well as tactile biofeedback (Hauser, 2005; Van Stan, Mehta & Hillman, 2015). Reported results are generally positive, but in most cases, results regarding retention were not reported. In addition, knowledge regarding principles of motor learning and how they may relate to practice and delivery of feedback is seldom incorporated in the study design.

1.4 MOTOR LEARNING THEORY

1.4.1 Principles of motor learning

Schmidt and Lee define motor learning as a set of processes associated with practice or experience leading to relatively permanent changes in the capability for movement (Schmidt & Lee, 2005). Learning can be roughly divided into two phases; acquisition and retention. The acquisition phase closely adheres to the training period. Changes in performance during, or directly after, practice are considered to be related to the acquisition phase. The retention phase, on the other hand, occurs after a period without practice. The amount of time needed to separate the acquisition and retention phase is not clearly established in the literature and can lead to varying interpretations of learning outcomes (Soderstrom & Bjork, 2015). Changes in performance observed hours, days, or preferably weeks or months after practice could be seen as evidence of retention of a learned behavior. Kantak and Winstein (2012) performed a review of the motor learning literature where learning outcome based on different practice and feedback conditions and both immediate

(same day) and delayed (>24 h) retention tests had been performed after the practice period. In 63% of the included studies (n = 41) there were inconsistent results between the immediate and delayed retention test. In 73% of the studies with inconsistent findings a significant difference between the different practice/feedback conditions could only be seen during the delayed retention test. Although not conclusive, their finding could be used as a basis for recommending that retention tests should be performed at least 24 hours after the end of practice to ensure that it is retention and not performance during acquisition that is being assessed. The different conditions of practice and different types of feedback that have been shown to affect the learning outcome are referred to as principles of motor learning. The primary principles of motor learning commonly described in motor learning literature are summarized in table 2.

Table 2. Summary of the primary principles of motor learning (Bislick, Weir, Spencer, Kendall & Yorkston, 2012). *Italicized* principles represent those that better facilitate retention of learned motor skills in contrast to improved acquisition with the exception of high number of trials which promotes both retention and acquisition.

Structure of Feedback	**Structure of Practice**
Knowledge of performance (feedback regarding specific aspects of the trial outcome)	Massed practice (practice in a short period of time)
Knowledge of results *(feedback regarding correctness of the trial outcome)*	*Distributed practice* *(practice over a long period of time)*
High-frequency feedback (I e, feedback after every trial)	Blocked practice (different targets in discrete blocks)
Low-frequency feedback *(I e, feedback after several attempts)*	*Random practice* *(different targets are presented randomly)*
Immediate feedback (feedback immediately following each trial)	Constant practice (practice in the same context)
Delayed feedback *(feedback provided with a delay)*	*Varied practice* *(practice in different contexts)*
	Low number of trials
	High number of trials

While motor learning has been studied extensively regarding gross motor function in general and limb motor function in particular, the research on speech motor learning is still somewhat limited. The interest and the amount of research being performed in the area

have however increased greatly in the last ten years (Bislick et al., 2012; Friedman, Hancock, Bamdad & Schulz, 2010; Iwarsson, 2015; Maas et al., 2008). The need to develop more structured and efficient treatment programs for childhood apraxia of speech has been a driving factor for some of the work (Hula, Robin, Maas, Ballard & Schmidt, 2008; Katz, McNeil & Garst, 2010; Maas, Barlow, Robin & Shapiro,2002; Maas, Gildersleeve-Neumann, Jakielski & Stoeckel, 2014; Preston, Leese & Maas, 2016). Other populations have been studied as well, including healthy speakers (Adams & Page, 2000; Kaipa, 2016; Steinhauer & Grayhack, 2000), individuals with PD (Adams & Page, 2000; Adams, Page & Jog, 2002) and aphasia (Knock, Ballard, Robin & Schmidt, 2000). Although limited, studies on applying principles on motor learning on speech motor learning have generally been promising in regard to confirming findings from the non-speech-motor learning literature.

1.4.2 Delivering feedback with a portable voice accumulator

By using a portable voice accumulator to deliver biofeedback, many of the general principles of motor learning that have been shown to facilitate a strong retention of a learned motor skill can be applied. The practice can easily reach a high number of trials as each utterance could constitute a trial. Practice can also be distributed over long periods of time. It can be randomized, as habitual speech can provide different and unique speech targets during conversation, or varied, depending on the context of the activities in which the speaker participates. The feedback that the available PVA:s deliver is provided in the form of knowledge of results. Their biofeedback activation signals only an incorrect production, such as too low a voice sound level. Depending on how the available adjustable biofeedback settings are configured, it would also be possible to provide low-frequency feedback. Of those components of motor learning described above that facilitate retention, delayed feedback is the only feature that cannot be provided by the PVA:s in their current form. The biofeedback signal occurs immediately after a trial and cannot be configured to be delayed.

1.4.3 Motor learning in Parkinson's disease

The capacity for motor learning in individuals with PD has been an area of significant interest for many years, since the basal ganglia have been shown to play a role in motor learning (Brasted & Wise, 2004; Graybiel, 1995; Graybiel, 2005). Findings have been inconsistent over the years, with earlier claims that acquisition and retention of motor skills might be impaired in PD (Agostino et al., 2004; Schulz, Sulc, Leon & Gilligan, 2000; Weiner & Singer, 1989). More recent studies have however reported results that show an intact motor learning potential for individuals with PD (Pendt, Reuter & Müller, 2011; Petzinger et al., 2013), but they might need increased practice through a higher number of trials and longer training periods (Niewboer, Rochester, Müncks &Swinnen, 2009).

As mentioned above, the feedback frequency is the main component of motor learning that can be directly configured in the PVAs available today. As with healthy individuals, in individuals with PD a reduced frequency of feedback has been shown to improve learning of a novel limb motor skill (Chiviacowsky, Campos & Domingues, 2010; Onla-or & Winstein, 2008), as well as of a speech task consisting of a reduced speech rate (Adams & Page, 2000; Adams et al., 2002). Contradictory findings were reported by Guadagnoli, Leis, Van Gemmert & Stelmach (2002) where the difference between 20% and 100% feedback was studied during training of a simple limb motor task. Twenty individuals with PD and 20 healthy controls where included in the study. Hundred percent feedback was reported to result in the greatest improvement in performance during retention tests; this differs from previous findings. However, the retention tests were carried out only 15 minutes after the end of practice, which might not be a sufficient time interval to separate acquisition from retention (Kantak & Winstein, 2011). The results could therefore be seen as confirming previous findings that a high-frequency feedback improves performance during the acquisition phase.

1.5 AIMS OF THE THESIS

The overarching aim of this thesis project was to increase the knowledge of how voice use and communication is affected in the daily life of individuals with PD. This included studying voice use as well as treatment outcomes in daily life using a portable voice accumulator in contrast to controlled studio environments. The aim was also to evaluate the biofeedback function available in the portable voice accumulator VoxLog as a possible alternate or complementary treatment option for individuals with PD and related hypophonia.

More specifically, the purpose was to:

- Compare voice use between patients with PD and matched healthy controls, both in daily life and in controlled studio environments. (Study I)
- Evaluate the treatment outcome in daily life of the leading speech and voice treatment (LSVT LOUD®). (Study II)
- Experimentally evaluate the biofeedback function available in the portable voice accumulator VoxLog, based on principles of motor learning. (Study IV)
- Evaluate the outcome following continuous biofeedback of voice sound level in habitual speech in daily life as a treatment alternative. (Study III & V)

2 MATERIALS AND METHODS

2.1 PARTICIPANTS AND RECRUITMENT

A summary of all 78 participants (56 individuals with PD and 22 healthy controls) included in the thesis is presented in table 3. Inclusion criteria for all participants with PD in study I-V were: diagnosis of idiopathic Parkinson's disease, subjective speech and voice symptoms and PD related hypokinetic dysarthria assessed by a speech and language pathologist. An additional criterion was that the participant or their partner should have no severe hearing impairment, as this would be expected to have an impact on the general voice sound level used.

Table 3. Participant characteristics for study I-V.

	n PD (male/female)	n Controls (male/female)	Mean age PD (male/female)	Mean age Control (male/female)
Study I	21 (11/10)	21 (11/10)	65.8 (66.6/65.0)	67.2 (68.0/66.4)
Study II	1 (1/-)	1 (1/-)	51.0	51.0
Study III	6 (5/1)	0	68.6 (69.6/64.0)	
Study IV	20 (13/7)	0	68.1 (69.2/66.1)	
Study V	8 (8/0)*	0	72.0	

*Sixteen participants were originally included.

The participants with PD were recruited through their clinical speech and language pathologist contact and through a national patient organization for individuals with PD. The control participants in study I where recruited through local retiree organizations and through the social networks of the individual's with PD. All participants underwent pharmacological treatment for their PD that was unchanged during the study period.

The inclusion criteria for the control group included no subjective voice symptoms, assessed with the Swedish version of the Voice Handicap Index (Ohlsson & Dotevall, 2009) with a cut-off-value of <20, no neurological disease with related speech or voice disorders and no severe hearing impairment for them or their partner.

Study II was initially planned as an intervention study to assess treatment outcome after LSVT LOUD® for a group of individuals with PD. The study design was however revised as a pseudo-single case design to allow for a more reasonable time frame within the

doctoral project. Participants were one individual with PD and one matched healthy control who was the patient's monozygotic twin. Their work and living conditions were similar, both living with a spouse and teenage children and working in manager positions with high demands on voice function.

Sixteen individuals were included and began participation in study V. During the participation period seven participants ended their participation early due to various reasons including the opportunity to receive in-patient rehab and sudden travel plans. Difficulties understanding how they should use the device and respond to the feedback was mentioned in a few cases and in some cases no reason was given as to why they wanted to withdraw from the study early. One of the eight participants who completed the program was female. As differences in voice function can be expected between men and women this participant was excluded from the analysis to allow assessment on a group level.

2.2 ASSESSMENT METHODS

2.2.1 The VoxLog

The VoxLog (firmware 2.2.3) is a portable voice accumulator, shown in figure 1, a device that enables long-term registration of voice use in daily life (Wirebrand, 2012). The VoxLog can register fundamental frequency, phonation ratio (percent time spent phonating during registration), voice sound level (dB) and the level of the background noise (dB). An accelerometer in combination with a microphone mounted in a plastic neck collar is used to detect phonation and monitor the voice parameters. The neck collar is connected to a box that can be worn in a pocket. During phonation, the device derives the fundamental frequency and phonation ratio from the skin acceleration at the neck generated by the activity in the vocal folds. When no phonation is detected, the microphone signal is registered as background noise, and when phonation is detected the microphone signal is registered as voice. Data can be registered continuously for up to one week before it must be downloaded to a computer with the software VoxLog Connect (version 3.1.18).

Figure 1. The portable voice accumulator VoxLog with accompanying neck collar.

2.2.2 Dysarthria assessment

Dysarthria assessment (in Swedish: Dysartribedömning) is a standardized clinical tool for assessment of respiration, phonation, oral motor function, articulation, prosody and intelligibility. It uses a four-point rating scale ranging from 0 to 3 (0: normal function to 3: severe deviation or no function) for each item. The mean score of all the sub-scales is calculated in a compound rating of dysarthria severity (Hartelius, 2015). The Dysarthria assessment by Hartelius (2015) was used in study V. An earlier version of the Dysarthria assessment (in Swedish Dysartritestet) with a five-point scale was used in study I-IV (Hartelius & Svensson, 1990).

2.2.3 Questionnaire on Acquired Speech Disorders

The Questionnaire on Acquired Speech Disorders (QASD, in Swedish: Självsvarsformulär om Förvärvade Talstörningar, SOFT) is a self-report questionnaire with items covering the speaker's subjective symptoms and experiences related to living with an acquired speech disorder. It includes three subscales; "my speech and language", "speech and language in social interaction" and "personal and environmental factors". It uses a four-point rating scale (0: definitely false to 3: definitely true) with a higher score representing more severe symptoms. QASD is a clinical tool developed in Sweden; its results have been shown to have a moderate-to-strong correlation with those of similar instruments that are more extensively used abroad (Hartelius et al., 2008; Hartelius, 2015).

2.2.4 Voice Handicap Index

The Voice Handicap Index (VHI, in Swedish: RöstHandikappIndex) is a self-report questionnaire containing 30 items, rated on a five-point scale (0: never to 4: always) covering three different dimensions of subjective voice symptoms. The sub-scales include physical, functional and emotional symptoms, each represented by ten items. A sub-score for each dimension is calculated in addition to the total score (0-120) (Ohlsson & Dotevall, 2009; Jacobsen et al., 1997).

2.2.5 Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) is a screening instrument for cognitive dysfunction. It consists of several tasks designed to assess different cognitive domains including attention and concentrations, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation. The maximum score is 30 points and 26 points represents a cut-off level for mild cognitive impairment (MCI) (Dalrymple-Alford et al., 2010; Nasredine et al., 2005).

2.3 PROCEDURES

Before participation, a standardized assessment protocol following clinical routine was administered to all participants in each of the five studies. This included the Swedish clinical dysarthria test, Dysarthria Assessment (Hartelius, 2015; Hartelius & Svensson, 1990) and the self-report questionnaire QASD which covers subjective symptoms and experiences related to living with an acquired speech disorder. All participants in study I and study V also rated their voice function with the Swedish version of VHI (Ohlsson & Dotevall, 2009). Figure 2 shows all VoxLog registrations performed in daily life, with the exception of study IV, in which VoxLog registrations were performed during semi-structured conversations in a clinical setting. Participants were given detailed instructions on how to wear and handle the VoxLog before beginning participation. Extra care was taken to instruct the participants on how to position the VoxLog collar to ensure proper placement and the positioning was evaluated during each visit to the lab.

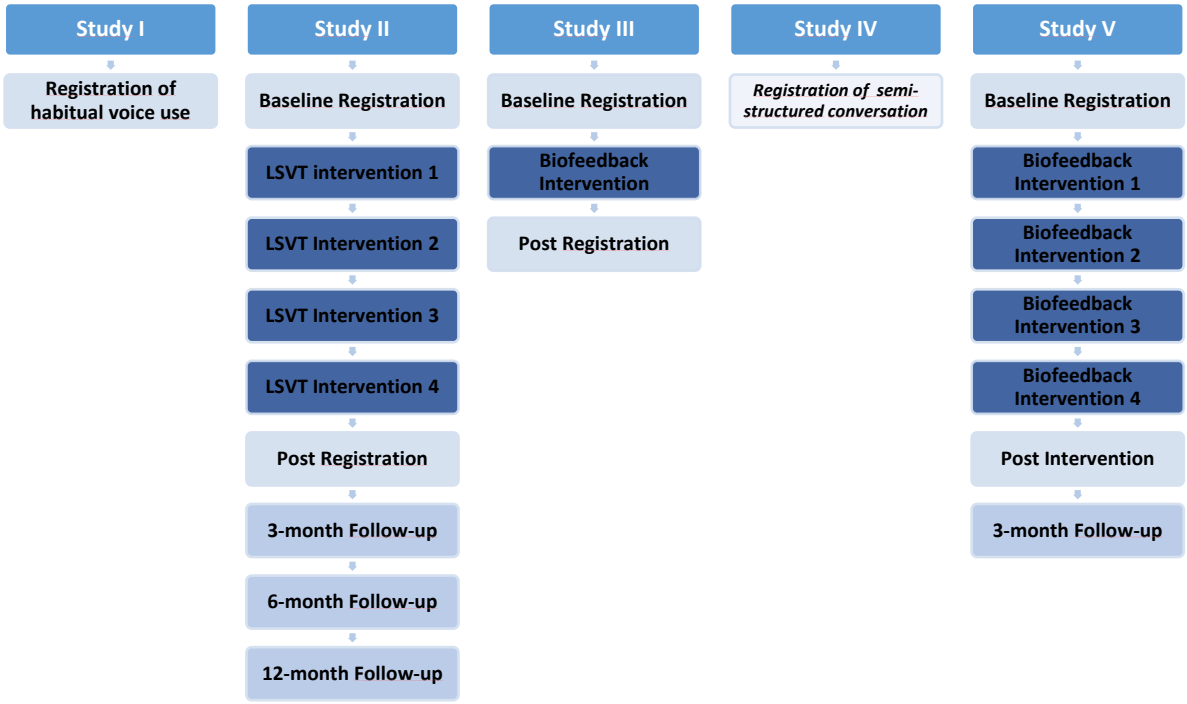

Figure 2. Flow-chart of VoxLog registrations performed in daily life. Each box represents one week of monitoring of voice use in daily life. Periods when intervention was given are shown in dark blue.

During all VoxLog registrations the participants were asked to note their activities during the day in a voice journal provided on paper in a binder. They were asked to write down the activities they had been performing during the day in general terms in boxes separated the

hours of the day. Especially if they had done anything out of the ordinary, for example participating in a large social gathering such as a dinner party or attending a concert. Voice data from time periods when activities had been performed that could be expected to not be representative of ordinary voice use was removed from the analysis, for example attending choir practice.

2.3.1 Study I

This study included long-term registration of voice use in uncontrolled settings in daily life as well as in a controlled studio recording setting. Participants in both groups, PD and control, wore the VoxLog during eight days during their daily activities. During the eight-day study period, the participants visited the research clinic three times; the first start-up visit, one control visit after three to five days, and a final visit after which participation ended. Voice use during a monologue speech task in a controlled studio recording environment was registered with the VoxLog on each visit to the clinic.

2.3.2 Study II

The participant with PD was treated with LSVT LOUD® for four weeks, which included a total of sixteen individual hour-long treatment sessions. Voice use was registered in daily life with the portable voice accumulator VoxLog, for a total of nine weeks during the participation period for the participant with PD. This included one baseline week prior to the start of LSVT LOUD®, four weeks during LSVT LOUD® and one week directly after finishing treatment, resulting in six continuous weeks of voice use registration. Week-long follow-up registrations were also performed at three, six- and twelve-months post LSVT LOUD®. During the baseline registration, the participant visited a speech and language pathology clinic three times: first for enrollment and giving consent to participate, after three days to control proper registration with the VoxLog and after a week to end baseline registrations and start the treatment program. Registrations of monologue speech in a controlled environment in a recording studio were performed with the VoxLog at each of the three visits during baseline. During the post treatment registration week and the three follow-up weeks (at three, six- and twelve-months post treatment), two clinic visits were performed to start and end registration of daily voice use and studio recordings were repeated at each visit following the same procedure as during baseline. The control participant performed the same long-term registration of voice use in daily life and controlled registrations in a recording studio during the baseline and follow-up week.

2.3.3 Study III

The participants in study III underwent a week-long intervention with biofeedback administered with the VoxLog. Voice use was registered for a total of three consecutive weeks, one baseline week, one intervention week and one follow-up week. Registration with the VoxLog of monologue speech in a controlled studio environment was performed once during the baseline week and once during follow-up. The threshold level for the biofeedback was individually configured based on the voice use registered during the baseline week. During the intervention week the participants wore the VoxLog during the whole day with biofeedback activated. The feedback signal was activated when the voice sound level went below the set threshold level.

2.3.4 Study IV

The aim of study IV was to assess how the VoxLog biofeedback function should be configured to provide a low-frequency feedback closest to twenty percent. Six different biofeedback configurations were assessed, based on the configurable parameters in the software VoxLog Connect. Two different activation time settings were used: 500 ms and 1000 ms, as well as three different threshold levels: 3, 6 and 9 dB SPL below the individual's mean voice sound level in habitual speech during baseline registrations. Baseline registration with the VoxLog of habitual voice use were performed for each participant during a 10-15 minute semistructured conversation together with the author (J.K.G.). Topics were prepared in advance and were chosen to encourage free discussion without too strong emotions; as sadness or anger, for instance, can be expected to impact the voice sound level used during conversation. Examples of topics were leisure activities, hobbies, work and travel experiences. After the baseline registration, six new semi-structured conversations with the different biofeedback configurations activated were performed. The biofeedback configurations were used in a randomized order between the different participants.

2.3.5 Study V

Study V was an intervention study in which the participants received biofeedback treatment with the VoxLog for four weeks. The biofeedback settings were individually adjusted based on the procedure recommended in study IV (Gustafsson, Södersten, Ternström & Schalling, 2016); settings used were a threshold level 3 dB below the voice sound level during baseline and an activation time of 500 ms. Voice use was registered for a total of seven weeks. Six consecutive weeks including one week of baseline registration, four intervention weeks where biofeedback was administered, and one week after intervention. Voice use was also registered during a follow-up week three months after the treatment period. The assessment and voice registration followed the same procedure as in study II where the treatment effect on habitual voice use in daily life was assessed during and following LSVT LOUD®. The

participants visited the speech and language pathology clinic three times during the baseline week for dysarthria assessment and three registrations of monologue speech in a controlled environment in a recording studio. Weekly control visits were performed during the four intervention weeks where the biofeedback settings were updated if the participant had changed their voice use in comparison to baseline. Registrations of voice use in a controlled environment following the same procedure as during baseline were performed at the beginning and end of the post intervention and three-month follow-up period as well.

2.4 ANALYSIS

2.4.1 VoxLog registrations

Data from the VoxLog registrations were downloaded to a computer using the accompanying software VoxLog Connect for all studies except study II (firmware 3.1.5 for study III, firmware 3.1.8 for study IV and 3.1.18 in study I & V). Using VoxLog Connect, the data can be visually presented in three graphs, showing phonation frequency, voice and noise sound level and phonation ratio for each registration day. The graphs of all registrations were visually inspected to identify if there were any incorrect registrations. These could be a result from malfunctioning electronics in the collar, a disconnected cable or that the participant forgot to power down the device when taking it off. The VoxLog Connect software can calculate mean values for the registration of voice sound level and noise sound level which was used for all studies. A different VoxLog software called VoxLog Discovery (firmware 1.0.14) was used for study II. VoxLog Discovery is an updated software with a more user-friendly interface but the older VoxLog Connect software was used in the subsequent studies as it allows for an easier process when backing up data. Data from a total of 127 weeks of continuous registration of voice use was collected in the studies that included field registrations; study I-III and V.

Further analysis was made of the data from the field registrations in study I and V, with the help of a custom Matlab script which calculated mean voice sound level, noise sound level and phonation ratio in three different noise ranges. The noise ranges used were based on the Swedish Work Environment Agency's recommendations concerning communication in noise (Arlinger, 1999) and can be seen in table 4. The custom Matlab script used also calculated self-to-other ratio (SOR) for the different noise ranges (Granqvist, 2003; Ternström, 1999;). Here, the SOR was defined as the difference between the uncompensated voice sound level and the noise sound level for the same time frame, as previously described by Szabo Portela, Granqvist, Ternström & Södersten (2018).

Table 4. Noise ranges

Noise range	dB range
Low levels of environmental noise	< 55 dB SPL
Normal levels of environmental noise	55 – 70 dB SPL
High levels of environmental noise	> 70 dB SPL

2.4.2 Statistical analysis

The statistical analysis in all studies was performed with IBM SPSS Statistics for Windows (IBM Corporation, Armonk, NY). Version 21 was used for study III and IV, version 23 for study II and version 25 for study I and V.

2.4.2.1 Study I

Repeated measures ANOVA was used to assess differences on a group level. The analyses included voice sound level and noise sound level for the whole week-long registration period as well as voice sound level, SOR and phonation ratio in different levels of environmental noise. Paired t-tests with a Bonferroni correction were used to study differences between the groups for the individual parameters.

2.4.2.2 Study II

Comparisons of voice sound level and noise sound level for the participant with PD and the control was made for the whole week-long registration periods and also separated into work and leisure time. Voice use was also studied in the different noise ranges described in table 5; however, this analysis was made by exporting the data from VoxLog Discovery to a spreadsheet program (Microsoft Excel), rather than by the automated Matlab script that was used for study I and V. The voice sound level and noise level were also split into thirty-minute segments and their correlation was calculated to assess the participant's ability to regulate voice sound level following variations in noise sound level. The correlation coefficients were also calculated for the week-long registration periods to assess whether variations in voice sound level following the intervention covaried with the variations in noise sound level. Spearman's rank correlation was used as some variables did not meet the assumption of normality, which was assessed using the Shapiro-Wilks test of normality.

2.4.2.3 Study III

Comparisons of voice use before, during and after intervention were made for the week-long periods, in both individuals and groups, for the parameters voice sound level, noise sound level and phonation time, using the paired samples t-test. The results regarding voice sound level were also separated by percentage phonated above or below the individually set threshold level for the different registration periods. Mean results for the monologue speech task during registrations in a controlled setting in a recording studio was presented for the registrations made before and after intervention.

2.4.2.4 Study IV

To assess the feedback frequency acquired from six different biofeedback settings, the data was exported from VoxLog Connect to Matlab (version R2012b). A custom Matlab script was then used to identify the number of biofeedback activations and the number of speech utterances. The quotient of the two gives the feedback frequency. A speech utterance was defined as a phonated time segment of >500 milliseconds followed by a silent period of >500 milliseconds. The participants naturally varied the voice sound level to some extent during the hour-long conversation, during which the different biofeedback settings were tested. As the threshold levels were based on the voice sound level used during the baseline registration, a correction quotient was calculated to achieve a corrected feedback frequency. The correction formula used was *(actual threshold level/predetermined threshold level) x acquired feedback frequency*.

2.4.2.5 Study V

Voice sound level and noise level were registered with the Voxlog for each of the seven weeks during participation; 1 baseline week, 4 intervention weeks, 1-week post intervention and 1 week at the three-month follow-up. Repeated measures ANOVA was used to assess differences in voice sound level and sound level on a group level over time. SOR was also studied in low, normal and high levels of noise. Linear regression analysis was performed to assess whether the changes in voice sound level after intervention could be interpreted as a result of the intervention or followed the variation in noise level. Regression analysis was also used to assess what effect screening results of cognitive function tested with MoCA had on the outcome in the difference in SOR after intervention.

2.5 ETHICAL CONSIDERATIONS

This project included recruitment of human participants which always involves challenging ethical considerations. One of the more unique aspects of this project is that the participants are asked to wear a portable voice accumulator, i.e. a device that registers voice use during

their daily activities outside the clinic for long periods of time. The VoxLog continuously registers the different voice parameters only; it never records the actual speech signal. This means that it is not possible to interpret or listen to what has been said during the registration period. This is very important for protecting the integrity of the participants and their conversational partners. It is however possible that wearing the visible device could lead to uneasiness for the participant. The participants were informed that they were allowed to end their participation at any time, without the need to give an explanation.

This brings up another important ethical consideration regarding recruitment of participants. The participants with PD were recruited through their clinical contact and were invited to participate in ongoing studies by their regular SLP clinician. Great care was taken to inform the participants that their regular clinical contact would not be affected by their decision to participate or not, or to end their participation if they felt that fulfilling the study tasks was not feasible. No participants received any financial compensation. The potential benefit from participating in the studies was mainly an opportunity to receive information and learn more about their individual voice function and voice use.

To ensure reliability and reproducibility, research is commonly performed in strictly controlled and defined environments, which also makes it easier to predict any complications or risks that could arise for the participant. In these studies, the participants were asked to wear research equipment in their daily life, inherently making complications harder to anticipate. To minimize risks when using the equipment, the participants were given very clear instructions on how to use and handle the device. For instance, participants were shown how to wear the VoxLog to minimize the risk of tangling up the cable connected to the collar. They were asked to wear the devices during as much time as possible during the day, and they were also carefully instructed to remove the device if they were going to perform activities where it would be unsafe to wear, e.g., during extraneous physical activity, showering, sleeping etc.

Another important aspect linked to recruitment of participants is the fact that cognitive symptoms are common in Parkinson’s disease. Both the verbal and written information given within the project had therefore been carefully designed to be easy to understand and interpret, so that participants could make an informed decision regarding participation.

3 RESULTS

3.1 VOICE USE IN PARKINSON'S DISEASE STUDIED WITH A PORTABLE VOICE ACCUMULATOR (STUDY I)

3.1.1 Voice sound level and environmental noise during a week-long registration period in daily life compared to registrations in a controlled environment

When comparing voice use in daily life between the individuals with Parkinson's disease and matched healthy controls, a significant difference in voice sound level could be seen for both the male and the female groups. The male individuals with PD used a mean voice sound level 6.1 dB lower than the control group ($p = 0.003$) and the female individuals with PD used a mean voice sound level 8.1 dB lower than the control group ($p = 0.001$). There was a non-significant difference in noise level for the male groups ($p = 0.401$). A significant difference in noise level was found for the female groups ($p = 0.025$), where the mean noise level was 4 dB lower for the individuals with PD. The mean difference in voice sound level and noise level, $diff_{voice/noise}$ for the individuals with PD was 13.9 dB for the male group and 15 dB for the female group. The mean $diff_{voice/noise}$ for the healthy controls was 17 dB for the male group and 19.1 for the female group.

The mean voice sound levels during monologue speech in a controlled studio environment and in habitual speech in daily life, in different noise ranges, can be seen in figure 3. A significant main effect between the control group and the individuals with PD could be seen for both the male participants ($p = 0.001$) and the female participants ($p = 0.001$). Both the control group and the individuals with PD consistently used a higher voice sound level in daily life compared to controlled studio recordings, even in low levels of environmental noise.

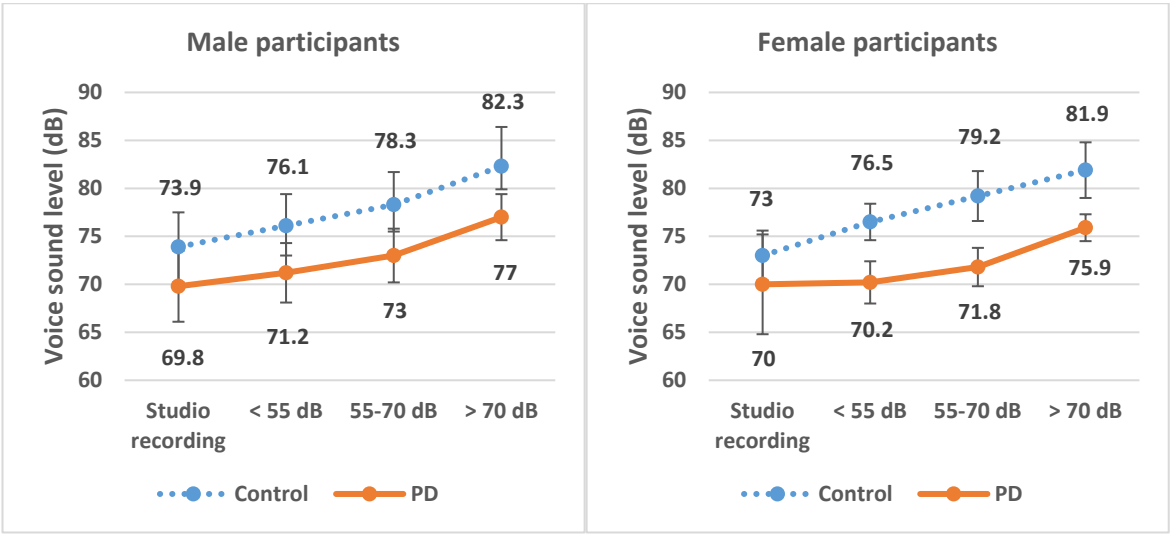

Figure 3. Average voice sound level (dB) during monologue speech during a studio registration and in different levels of environmental noise during long-term registration in daily life, for all participants, separated by group and sex (n male PD group = 11; n male control group = 11; n female PD group = 10; n female control group 10.). Bars denote +/- standard deviation.

3.1.2 Self-to-Other Ratio during a week-long registration period in daily life

Figure 4 shows the SOR in different levels of environmental noise for all participants separated by gender and group. There was a significant main effect between the control group and the individuals with PD for both the male participants ($p = 0.001$) and the female participants ($p = 0.001$).

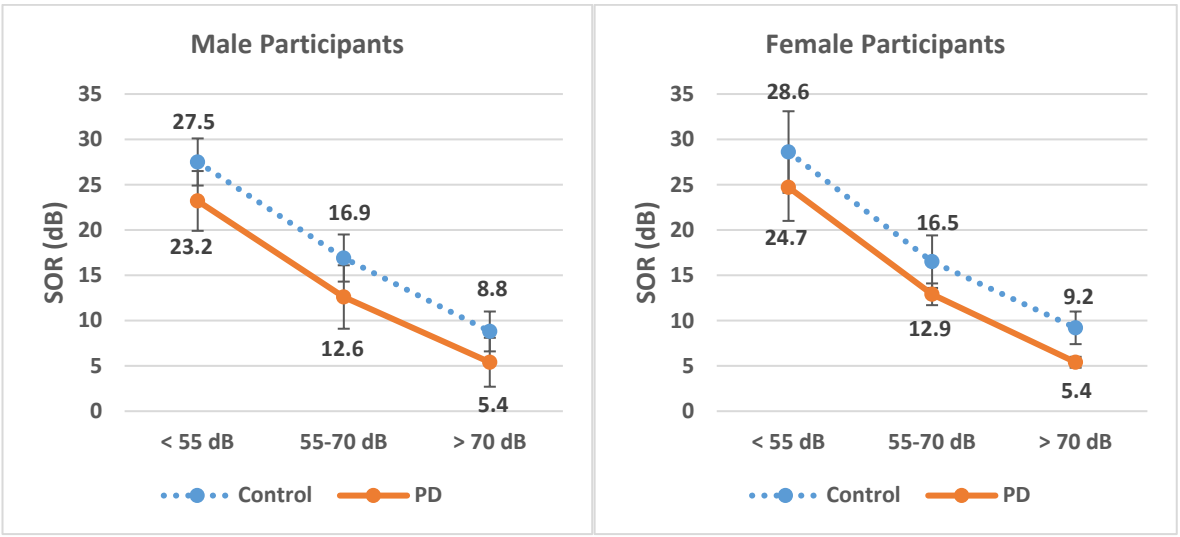

Figure 4. Self-to-other ratio (SOR) in different levels of environmental noise during long-term registration in daily life for all participants divided by group and sex (n male PD group = 11; n male control group = 11; n female PD group = 10; n female control group 10.). Bars denote +/- standard deviation.

3.1.3 Phonation ratio during a week-long registration period in daily life

Both male and female individuals with PD used their voice significantly less on a group level compared to matched controls. The male group with PD had a phonation ratio 50% lower than the control group ($p = 0.001$). The corresponding difference for the female group with PD was 60% less phonation ratio than the control group ($p = 000.1$). When studying the phonation ratio in different ranges of noise levels, a significant interaction effect could be seen ($p = 0.031$ for the male groups and $p = 0.011$ for the female groups); individuals with PD used their voice less in high noise levels, as can be seen in figure 5.

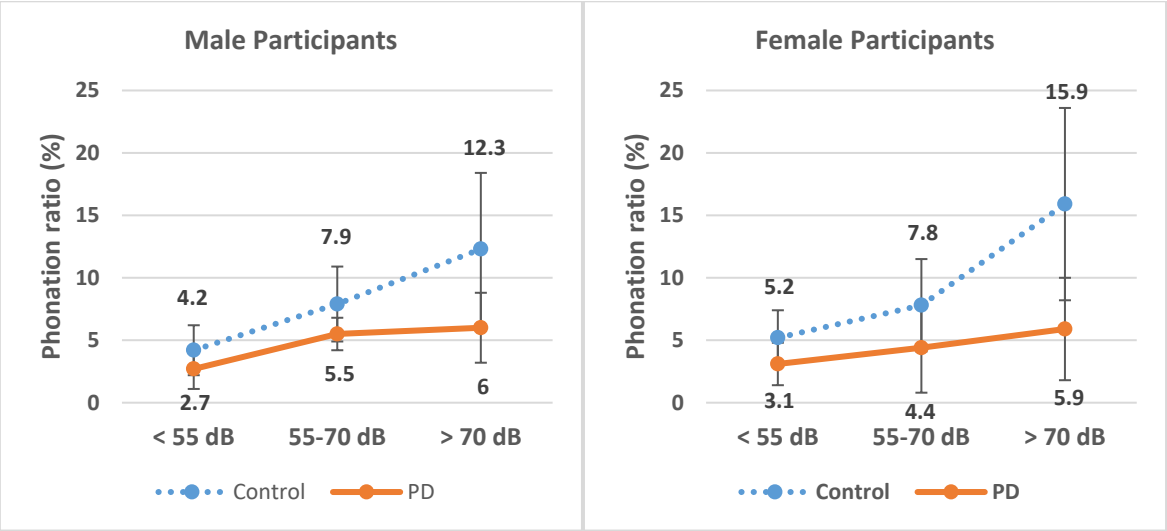

Figure 5. Phonation ratio (percent) in different levels of environmental noise during long-term registration during daily life for all participants divided by group and sex (n male PD group = 11; n male control group = 11; n female PD group = 10; n female control group 10.). Bars denote +/- standard deviation.

3.2 OUTCOME AFTER LSVT LOUD® STUDIED WITH A PORTABLE VOICE ACCUMULATOR (STUDY II)

The individual with PD who underwent LSVT LOUD® intervention increased his mean voice sound level by 4.1 dB in the week after intervention, compared to the baseline week when measured with the VoxLog during daily voice use. During monologue speech in a controlled lab environment, the increase after intervention was 5.6 dB. The difference in voice sound level and noise level, $diff_{voice/noise}$ was 20.2 dB during baseline and 24.2 dB in the week post intervention. At the three-month follow-up, the difference in voice sound level compared to baseline was 3.5 dB while $diff_{voice/noise}$ was 17.8 dB. The difference in voice sound level compared to baseline was 2.3 dB at the six-month follow-up, with a $diff_{voice/noise}$ of 18.5 dB. At the one-year follow up, the difference in voice sound level compared to baseline was 1.4 dB and the $diff_{voice/noise}$ was 20.4 dB.

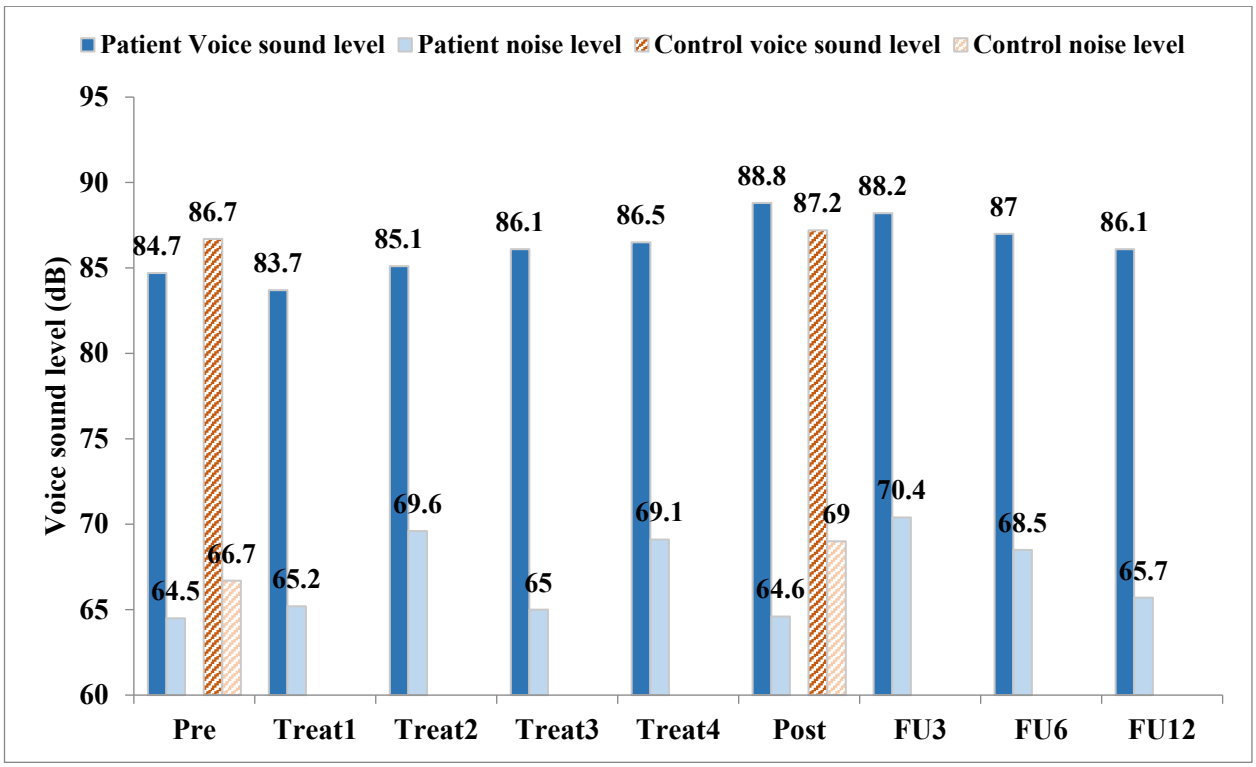

Figure 6. Mean voice sound level and mean noise sound level during the whole week-long monitoring periods for both participants. The mouth-to-microphone distance was approximately 10 cm.

To assess whether variations in noise level explained the variations in voice sound level, the correlation between voice sound level and noise level was calculated over all registration periods. No significant correlation was found for the individual with PD, Spearman's rho = 0.25 ($p = 0.515$). A significant correlation was however found for the control participant, Spearman's rho = 0.94 ($p = 0.005$).

Table 5. Correlations between the participants' L_{voice} and the L_{noise} within respective registration period including pretreatment, post treatment and at follow-up (FU) three, six, and twelve months post treatment.

Period	Spearman's rho	*p*-value
Individual with PD - Pre	0.53*	0.000
Individual with PD - Post	0.28*	0.032
Individual with PD - FU3	0.64*	0.000
Individual with PD - FU6	0.60*	0.000
Individual with PD - FU12	0.58*	0.001
Control – Pre	0.83*	0.000
Control – Post	0.79*	0.000

*Significant correlation ($p < 0.05$).

Correlation was assessed also on 30-minute segments for the whole registration period, to study how well the participants regulated their voice sound level in response to variations in noise. Table 5 shows the correlation coefficients and p-values for all periods.

3.3 BIOFEEDBACK DELIVERED WITH A PORTABLE VOICE ACCUMULATOR (STUDY III-V)

3.3.1 Outcome after a single-week biofeedback intervention (Study III)

A significant mean increase of 1.5 dB in voice sound level was seen during the intervention week compared to during the registrations the week before intervention ($p < 0.05$). The difference in mean voice sound level after the intervention week compared to baseline or compared to the intervention week was not significant. There was no significant difference in noise level between the different registration periods. The $diff_{voice/noise}$ for the pre intervention week was 13.6 dB, 15.1 for the intervention week and 12.9 dB during the post intervention week.

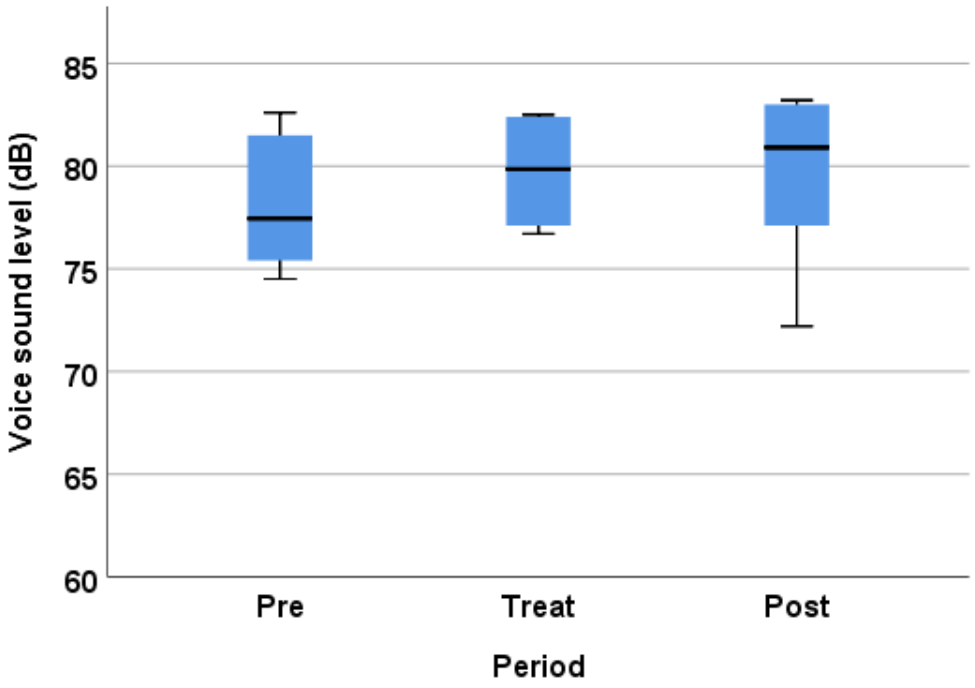

Figure 7. Box plots presenting voice sound level for the three registration weeks for the group of participants (n = 6). The line shows the median, the boxes the first and third quartile and the bars denote 95% confidence intervals.

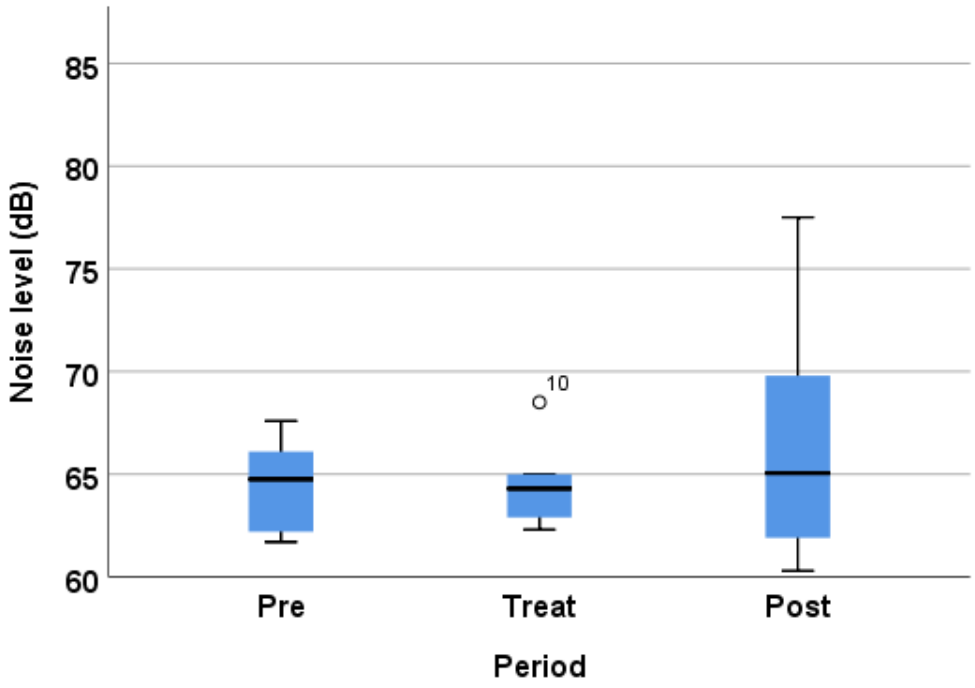

Figure 8. Box plots presenting noise level for the three registration weeks for the group of participants (n = 6). The line shows the median, the boxes the first and third quartiles, and the bars denote 95% confidence intervals, outliers are shown with a separate circle.

3.3.2 Methodological development (Study IV)

The six different biofeedback settings (two different activation times; 500 and 1000 msec, and three different threshold levels; 3/6/9 dB below mean voice sound level) resulted in a feedback frequency range of 0 - 49.8%. Figure 9 show mean feedback frequency for each setting and the corresponding 95% confidence intervals. The feedback setting that resulted in a feedback frequency closest to 20% was a threshold level 3 dB below mean voice sound level and an activation time of 500 msec.

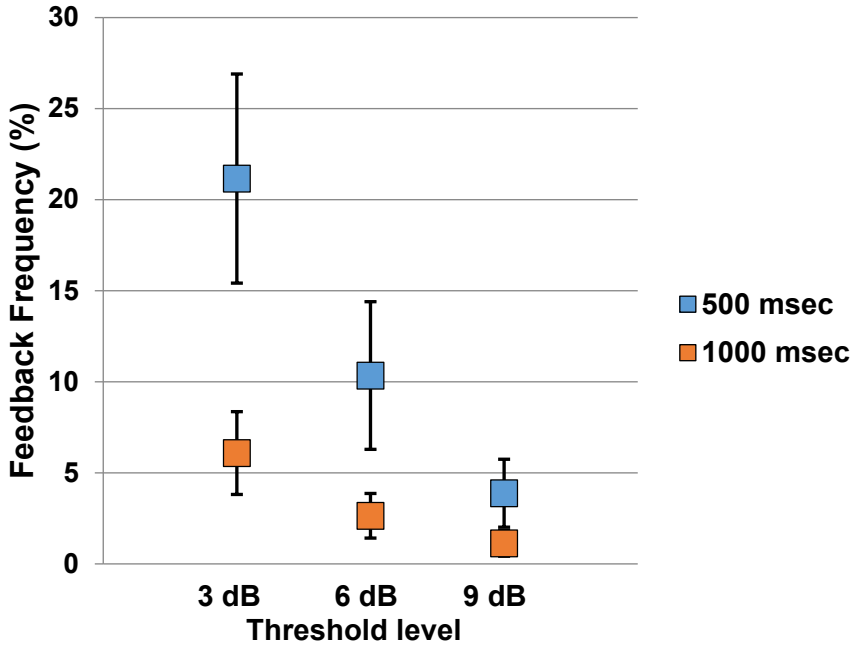

Figure 9. The figure shows 95% confidence intervals showing feedback frequency for the different feedback settings.

3.3.3 Outcome after a four-week biofeedback intervention (Study V)

A mean increase of 1.6 dB in voice sound level was seen the week post intervention compared to the week pre intervention for the group of 8 participants. The corresponding increase during the follow-up registration was 1 dB. Comparing voice sound level and noise sound level for each period, $diff_{voice/noise}$, the mean difference was 12.5 dB during the pre-intervention registration period, 16.3 dB during the post intervention period and 16.5 dB during the follow-up period. The differences between the pre/post and pre/follow-up periods were significant ($p > 0.05$ in both cases).

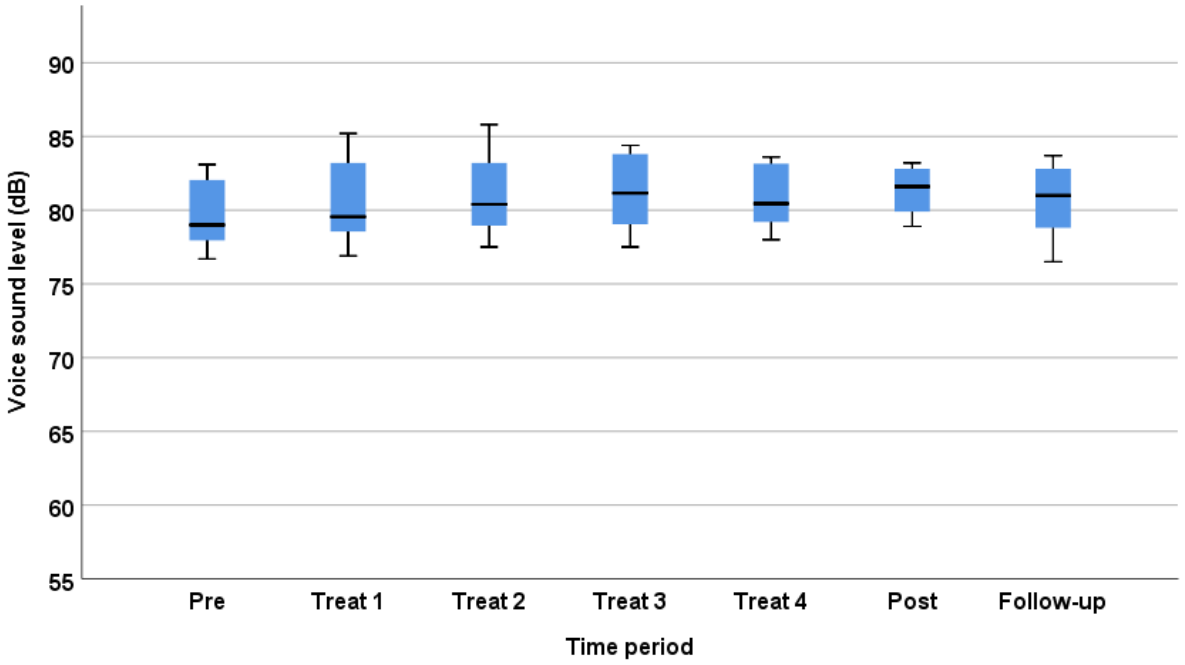

Figure 10. Box plots presenting voice sound level for the seven registration weeks for the group of participants (n = 8). The line shows the median, the boxes the first and third quartile and the bars denote 95% confidence intervals.

The changes in voice sound level over all periods could not be significantly predicted by the variations in noise level in a linear regression analysis ($r^2 = 0.068$, $p = 0.053$).

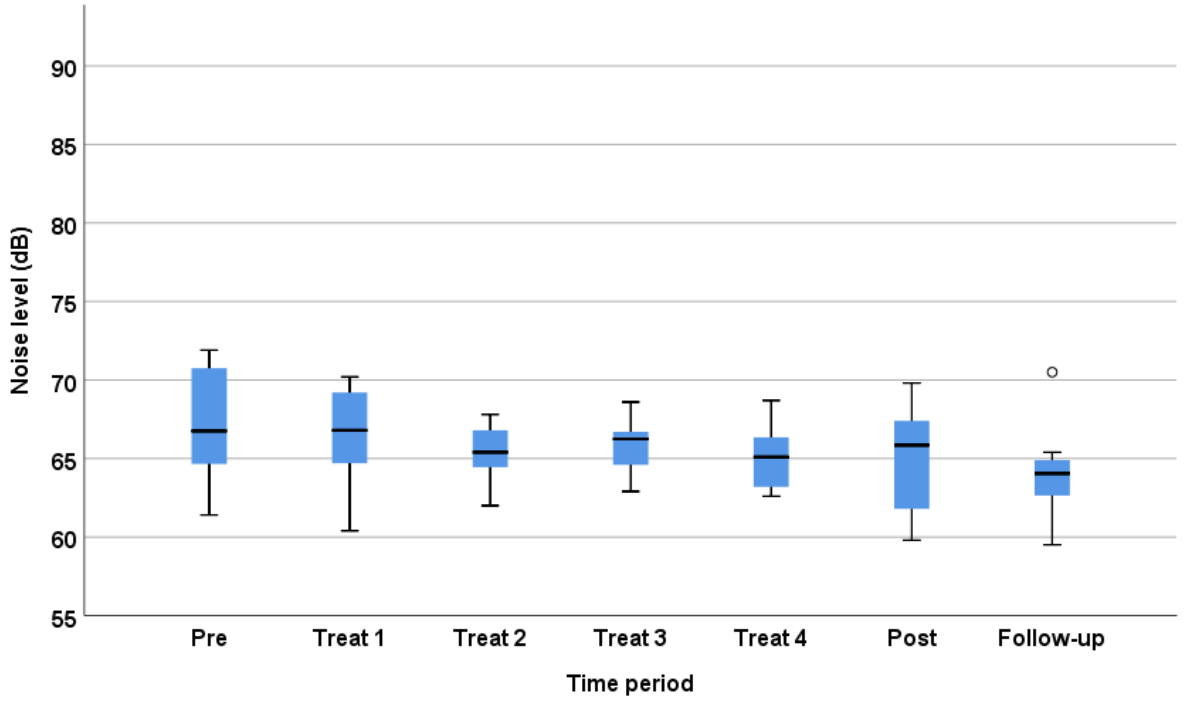

Figure 11. Box plots presenting noise level for the seven registration weeks for the group of participants (n = 8). The line shows the median, the boxes the first and third quartile and the bars denote 95% confidence intervals, outliers are shown with a separate circle.

The SOR in different noise ranges for the periods pre-intervention, post intervention and follow-up (box plots shown in figure 12) exhibited no significant differences between the different periods at the group level ($p > 0.05$ in all cases). However, a distinction could be seen between four individuals who scored above the cut-off for MCI on the cognitive screening with MoCA (≥26 points) and four individuals who scored below the cut-off level (≤26 points). The group who scored within normal levels saw a more positive treatment outcome with generally increased SOR during follow-up compared to pre-intervention, while the pattern was reversed for the group with MoCA scores below normal levels (individual values shown in figure 13 and 14). A linear regression analysis showed that MoCA scores significantly predicted SOR outcome with 92.4% explained variability in normal noise ranges ($p = 0.001$) and 87.6% explained variability in high noise ranges ($p = 0.001$).

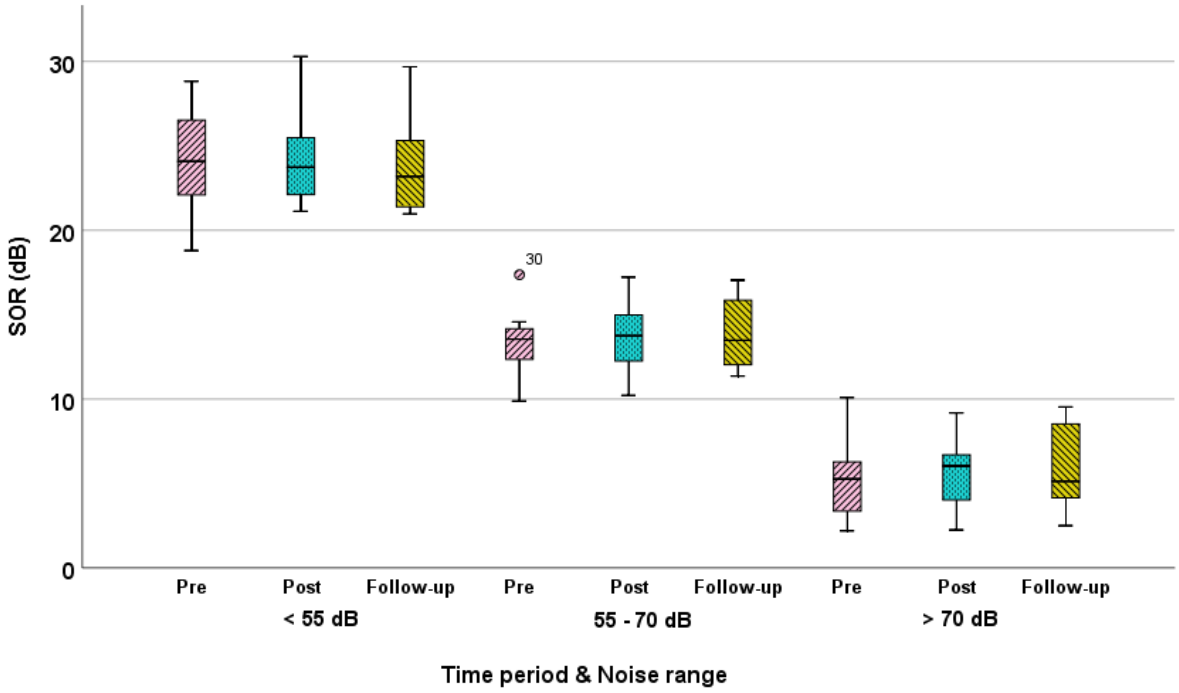

Figure 12. Box plots showing the Self-to-Other Ratio for the different noise ranges and the pre, post and follow-up week for the group of participants (n = 8). The line shows the median, the boxes the first and third quartile and the bars denote 95% confidence intervals, outliers are shown with a separate circle.

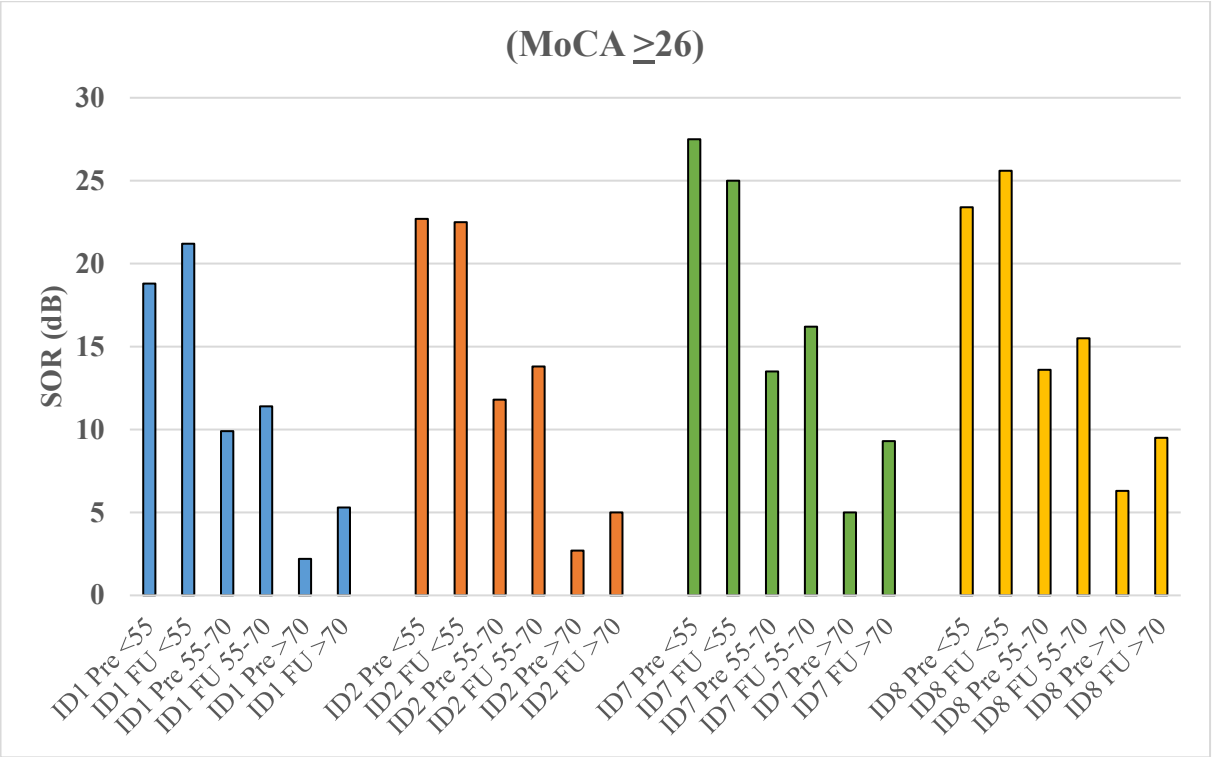

Figure 13. Diagram showing the mean Self-to-Other Ratio in the different noise ranges for the four participants (Id 1, 2, 7, 8) with a MoCA score ≥ 26 before intervention (Pre) and at three-month follow-up (FU).

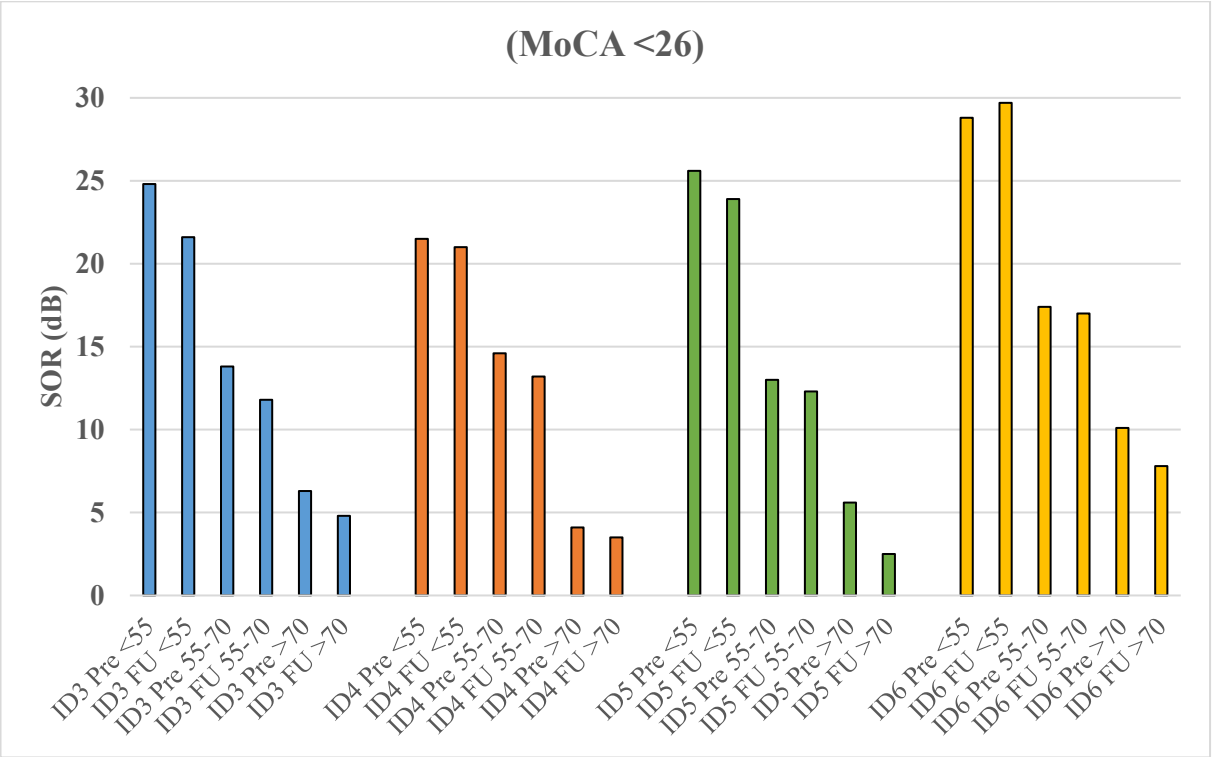

Figure 14. Diagram showing the mean Self-to-Other Ratio in the different noise ranges for the four participants (Id 3, 4, 5, 6) with a MoCA score < 26 before intervention (Pre) and at three-month follow-up (FU).

4 DISCUSSION

In this thesis, the impact of PD on the individual's ability to communicate has been explored using methods to study voice use in daily life. The portable voice accumulator VoxLog, used in all the studies included in the thesis, also has a biofeedback function that can be used for a therapeutic purpose. Further goals of the thesis have been to assess outcomes after traditional voice treatment for individuals with PD, LSVT LOUD®, and to test, develop and evaluate biofeedback intervention using the VoxLog. The studies included in this thesis are the first to objectively assess voice use in daily life in individuals with PD. How daily communication, voice function and voice use are affected by PD is of particular interest, since a discrepancy between voice use in controlled environments and in daily life could be expected to be high following the various motor and non-motor symptoms common in PD.

4.1 WEARABLE TECHNOLOGY AND ECOLOGICAL VALIDITY

The use of PVAs to study voice use in a setting closer to the speaker's daily life dates as far back as the seventies, when Holbrook, Rolnick & Bailey (1974) used a portable device to monitor voice intensity for individuals with vocal fold lesions and hyperfunction. Despite the vast technological advancements made in the decades since then, there are still no portable or wearable devices commonly used in clinical practice related to voice disorders. When work started on this thesis project, there were mainly two portable voice accumulators commercially available; the VoxLog and the Ambulatory Phonation Monitor, developed both with research and clinical use in mind. A device specifically made for clinical use, the VocaLog, was soon introduced. The VoxLog is not commercially available at the present date, and a few new devices have been developed around the world, mainly with a research focus, such as the Voice Health Monitor (Mehta et al., 2015) and the Voice Care (Astolfi, 2016a; Astolfi, 2016b). The use of wearable technology to study voice use does provide a method to fill in an important knowledge gap in voice research and therapy. Voice function is traditionally studied in controlled environments to ensure validity and replicability or through subjective ratings of voice use. Quantitative data on voice use in settings outside controlled clinical settings are lacking. The findings from study I showed significant differences in voice use between the group with PD and the healthy controls regarding voice sound level and phonation ratio in different noise ranges. Voice use is, as hypothesized, different in daily life compared to recordings in a controlled environment.

4.2 CHANGES IN VOICE USE IN INDIVIDUALS WITH PD

A wide variety of both objective and subjective changes in voice function, voice use and communication following PD have been described (Duffy, 2013; Baylor et al., 2011; Miller et al., 2006). One of the most prominent is of course a decreased voice sound level, leading to difficulties making oneself heard.

4.2.1 Changes in voice sound level following PD

Voice use in daily life was examined for individuals with PD and matched healthy controls in study I. Significant differences in voice sound level were found between the groups, for both the male and female participants. The female group of individuals with PD used a mean voice sound level that was 8.1 dB lower than their matched healthy controls during one week of monitoring with the VoxLog in daily life. For the male group of individuals with PD, the mean voice sound level was 6.1 dB lower than the matched group of healthy controls. The difference in voice sound level between individuals with PD and healthy controls have been studied earlier by Fox and Ramig (1997), although in a controlled studio setting and not in daily life. In different speech tasks including sustained vowel phonation, reading and monologue speech during a controlled studio recording, individuals with PD had an average voice sound level that was 2-4 dB lower than the healthy controls (Fox & Ramig, 1997).

The reduced voice sound level in PD can be explained as an effect of the hypokinesia and rigidity characteristic for PD. Hypokinesia, implying decreased amplitude of movements, and rigidity can be expected to impact both respiratory, laryngeal and articulatory movement leading to a reduced voice sound level (Baker, Ramig, Luschei & Smith, 1998; Duffy, 2013; Fox et al., 2002; Luschei, Ramig, Baker & Smith, 1999; Pfann, Buchman, Cornella & Corcos, 2001). The non-motor symptoms related to PD could however be a strong contributing factor as well. Changes in central sensory processing have been reported to create difficulties for self-regulating the voice sound level in response to internal cues, and to decrease awareness of the speakers own soft voice (Arnold, Gehrig, Gispert, Seifried & Kell, 2014; Clark, Adamas, Dykstra, Moodie & Jog, 2014; Guehl et al., 2008; Ho et al., 2000; Houde et al., 2004; Kwan & Whitehill, 2011; Mollaei, Schiller & Gracco, 2013; Liu, Wang, Metman & Larson, 2012; Sapir et al., 2014). The increased difference in voice sound level between individuals with PD and healthy controls seen in study I and study II compared to earlier reports by Fox and Ramig (1997) might be a result of this as well. Unlike the studio, there are in daily lifemany distractors that increase the cognitive load, leaving less energy and focus for speech production. These factors include variations in noise, stress, physical movement and emotional state, and possibly others. An example of a clinical representation of this, familiar to many with experience of working with patients with PD, is to observe the patient walking from a clinic waiting room to the clinician's office. The patient's voice sound level is often stronger during the greeting in the waiting room, which is short and concise, and while sitting down in the clinician's office, where the noise is reduced and no physical movement is involved, compared to during the walk to and from the office where noise, movement and postural balance increases the cognitive load. In many cases, conscious or unconscious compensatory strategies are used, such as keeping silent or refraining from talking.

4.2.2 Impact of environmental noise on voice sound level

Variations in noise level are known to lead to a somewhat unconscious regulation of voice sound level (Lombard, 1911). This phenomenon has also been studied in individuals with PD and it has been shown that individuals with PD react to variations in noise level in a pattern similar to that in healthy speakers on a group level (Adams & Lang, 1992; Dromey & Adams, 2000; Ho, Bradshaw, Ianseck & Alfredson, 1999; Sadagopan & Huber, 2007; Stathopoulos et al., 2014). The findings in study I and II confirm these earlier results, according to which increasing noise levels leads to increasing voice sound levels during speech in daily life. Even though based on only one pair of participants, there was a difference between the individual with PD and the matched control in study II such that the correlation between variations in noise level and regulation of voice sound level was stronger for the control participant during the registration period before intervention started; Spearman's rho = 0.81 for the control and Spearman's rho = 0.53 for the individual with PD. In this single pair of participants both of them regulated their voice sound level in response to changes in noise level, but the healthy speaker did so to a greater extent.

4.2.3 Changes in phonation ratio following PD

Limitations in communicative participation are commonly reported by individuals with PD (Baylor et al., 2011; Miller et al., 2006). The results from study I show that the matched healthy controls used their voice 50-60% more than the individuals with PD on a group level. The phonation ratio represents the percentage time spent phonating during the registration period. It might be used to quantify objectively the communicative participation, which inherently is something quite subjective. It is difficult to know whether the lower phonation ratio is a result of the individuals with PD taking a less active role in communication, or if the difference is related to individuals with PD being less communicative situations because of the physical impairments making it more challenging to take part in social gatherings altogether; as reported by Sjödal Hammarlund, Westergren, Åström, Edberg & Hagell (2017). An interesting finding in study I on this topic is that an interaction effect was found, showing that individuals with PD do not increase their phonation ratio in situations with high environmental noise, which was the case for the control groups. A situation or environment with high noise levels is in many cases a social situation, for example a restaurant, café or dinner party, where communication naturally occurs more frequently. This would explain why the phonation ratio increased in high noise ranges for the control groups. That a similar pattern was not seen for individuals with PD could suggest that they were not as active in such situations as their healthy controls.

4.3 INTERVENTION AND HYPOPHONIA RELATED TO PD

The changes in central sensory processing and internal cueing deficits in PD may be one contributing factor to why the hypokinetic dysarthria common in PD generally does not respond to pharmaceutical or surgical intervention methods that primarily target the dopamine deficiency (D'Alatri et al., 2008; Ho et al., 2008; Pinto et al., 2005; Plowman-Prine et al., 2009; Ramig et al., 2007; Schulz et al., 2012; Skodda et al., 2010; Skodda et al., 2012). The limited and variable effect on speech and voice symptoms from pharmaceutical and surgical treatment have made behavioral approaches the main treatment option for dysarthria and hypophonia in PD. Study II aimed to examine the outcome from the leading voice therapy option, LSVT LOUD®, through assessing changes in voice use in daily life with the help of the PVA VoxLog. Initially planned as group trial, it was later revised to a pseudo-single case study with a matched healthy control to better fit the scope of the present thesis project.

In study II, a 4.1 dB increase in voice sound level averaged over one week was seen for the individual with PD after LSVT LOUD® intervention, compared to the baseline week voice sound level. For monologue speech during a controlled studio recording the corresponding increase after intervention was +5.6 dB. This increase was comparable to previously reported outcomes in a similar context: mean +4.7 dB by Ramig et al. (2001) and mean +5.2 dB by Ramig et al. (2018). A greater improvement during a defined speech task during a controlled recording (5.6 dB increase) compared to field recording (4.1 dB increase) was expected as there are fewer distractors competing with the focus on speech production. A gradual decline in the retained treatment effect on voice sound level was seen during the follow-up periods as follows: directly post intervention: 4.1 dB above baseline, three-month follow-up: 3.5 dB, six-month follow-up: 2.3 dB, twelve-month follow-up: 1.4 dB. The change in voice sound level during monologue speech during registration in a studio environment at twelve-month follow-up was 3.8 dB compared to baseline in study II. In the study by Ramig et al. (2018) follow-up was made at seven months and the mean difference in voice sound level during monologue speech was 2.8 dB. Ramig et al. (2001) performed follow-up recordings of monologue speech after 24 months and the difference in voice sound level compared to baseline was 2.3 dB. The decay of treatment effect, or disease progression, follows a similar pattern in all studies, both during controlled recordings and during voice use in daily life.

4.4 BIOFEEDBACK INTERVENTION FOR HYPOPHONIA RELATED TO PD

The clinical experience of some individuals with PD showing positive outcome with increased voice sound levels during speech tasks in a controlled environment after voice treatment, yet still struggling with the transfer to voice use in daily life gave the impetus to this thesis work. Being able to provide real-time biofeedback regarding voice sound level in daily life is promising for individuals with PD, since the training happens in the context where change and improved voice function are desired. And, considering the deficiencies in

internal queuing previously described, providing an external que through the biofeedback should promote a new motor behavior for the group. The use of external biofeedback has been shown earlier to have positive results for individuals with PD albeit in a controlled practice setting (Laukkanen et al., 2004; Le Dorze et al., 1992; Norrlinder & Olsson, 2009; Sadagopan & Huber, 2007; Schneider-Stickler et al., 2012; Scott & Caird, 1983).

The aim of study III was therefore to evaluate the effects of a one-week intervention where individuals with PD received continuous biofeedback of voice sound level in daily life. The hypothesis was that receiving continuous feedback on the target behviour (habitual speech in daily life) with the help of external biofeedback should promote generalizability. An increase in voice sound level (1.5 dB) and $diff_{voice/noise}$ (1.4 dB) was seen during the intervention compared to baseline but the effect was not retained when the biofeedback period stopped (increased voice sound level of 1.3 dB but a decreased $diff_{voice/noise}$ of -0.7 dB). The participants reported that using the device helped them become more aware of how they were using their voice and, in some cases, inquired about the possibility to use the device as a technical aid. This led to the planning of study IV in which the biofeedback configuration was experimentally tested to find settings likely to promote retention of learned behavior based on principles of motor learning. The results from study IV where then used in study V in which an extended biofeedback intervention was evaluated. A four-week long intervention period was used to match the intensity of practice that LSVT LOUD® offers.

The results from study V showed a mean increase in voice sound level of 1.6 dB the week after intervention compared to the week before intervention. The corresponding difference at three-month follow-up was 1 dB. When taking variations in noise level into account the $diff_{voice/noise}$ was 3.8 dB after intervention compared to before. At the three-month follow-up the difference was 3 dB. Comparing the results with the one-week biofeedback intervention the four-week intervention had a more successful outcome, indicating that a longer, more intensive, practice period was needed to achieve retention of the improved skill. In study II, in which the participant with PD underwent LSVT LOUD®, a greater increase in voice sound level of 4.1 dB in daily life was seen during the week post intervention together with a comparable increase in $diff_{voice/noise}$ of 4 dB. At the three-month follow-up the outcome seen in study II was a 3.5 dB increase in voice sound level, but a -2.4 dB decrease in $diff_{voice/noise}$,as compared to the baseline. In study V, at the three-month follow-up the increase in voice sound level was 1 dB but an increased $diff_{voice/noise}$ of 3 dB was seen on a group level. This could be interpreted as a more positive outcome following the four-week biofeedback regarding the ability to make oneself heard above the noise level. However, the $diff_{voice/noise}$ at three-month follow-up was 16.5 dB and 17.8 dB respectively. Arlinger (1999) proposed that a $diff_{voice/noise}$ of 15 dB is needed to easily be heard above the noise level. With that in mind, a further increased $diff_{voice/noise}$ might not have been needed for the individual with PD in study II.

4.5 MOTOR LEARNING AND PD IN RELATION TO BIOFEEDBACK INTERVENTION

The basal ganglia, where the dopaminergic deficiency resulting in PD originates, have been shown to play a critical role in motor learning (Brasted & Wise, 2004; Graybiel, 1995; Graybiel, 2005). There were early suggestions that individuals with PD might be resistant to behavioral treatment (Weiner & Singer, 1989) and that the capacity for motor learning and generalization have been impaired (Agostino et al., 2004; Schulz et al., 2000). These notions have been challenged in recent years (Niewboer et al., 2009; Pendt et al., 2011; Petzinger et al., 2013), not least in view of the positive outcomes after intervention for example shown in studies of LSVT LOUD® (Ramig et al., 2001; Ramig et al., 2018).

Providing real-time, continuous biofeedback on voice sound level in daily life could in many ways be motivated as the ideal way to promote a change in motor behavior for individuals with PD. A majority of those principles of motor learning that have been shown to facilitate retention of an improved motor skill after training (described in table 3) are achieved when biofeedback is delivered by a PVA that is monitoring the individuals' habitual speech during their daily activities. The feedback provided through the VoxLog can be configured to provide a *low-frequency feedback* and it comes in the form of *knowledge of results* as the vibration is triggered only if the voice sound level goes below the set threshold level. Depending on the training period, the practice can be *distributed* over time and a *high number of trials* can be achieved. The speech target is habitual speech in daily life which inherently provides a *randomized* practice as new and ever-changing utterances are produced in communication and the practice becomes *varied* as different contexts are offered continually. With the settings that are configurable in the VoxLog practice cannot be presented in a *delayed* manner; the feedback can be provided only *immediately*. In summary, all principles of motor learning promoting retention except one can be achieved when trying to promote lasting change in motor skill through training with biofeedback provided by the VoxLog.

An additional benefit of providing real-time biofeedback on habitual voice use in daily life is that the deficits in central sensory processing and internal cueing can be addressed with this method (Arnold et al., 2014; Clark et al., 2014; Guehl et al., 2008; Ho et al., 2000; Houde et al., 2004; Kwan et al., 2011; Liu et al., 2012; Mollaei et al, 2013; Sapir et al., 2014). The biofeedback signal provides an external cue that could help the individual with PD regulate the voice sound level more efficiently than when relying solely on internal cues.

4.6 COGNITIVE FUNCTION AND BEHAVIORAL TREATMENT IN PD

The results from study V showed that individuals who scored at or above the cut-off level for MCI on the cognitive screening tool MoCA had a better outcome after biofeedback intervention than the group who scored below the cut-off level for MCI. The lack of lasting results for the group with lower MoCA scores could be a consequence of difficulties in managing the technical aspects of using the VoxLog and how to respond to its biofeedback signal, or perhaps of increased difficulties using internal cues to regulate voice sound level after the biofeedback was removed. Attention deficits related to PD could affect also the ability to notice and respond to the biofeedback signal (Dujardin et al., 2013). Many of the participants who did not complete the whole participation period in study V reported that managing the device was cumbersome, leading to the interpretation that this could have been the case for those with lower MoCA scores who completed the participation in full as well. Screening of cognitive function is be recommended in future studies that employ technical aids such as a PVA to provide biofeedback for individuals with PD.

4.7 METHODOLOGICAL DISCUSSION

All participants with PD where consecutively recruited to participate in the studies through the participants own initiative after receiving information through their clinical contact or local patient organizations. In many cases there will be a certain type of individual who shows interest in participating in studies that involves active participation. One can expect such individuals to be more active and be in an earlier stage of the disease progression as it demands energy and commitment to participate. This can be seen to a large extent in the participant characteristics in the different studies. A majority were rated to have a mild hypokinetic dysarthria and only a few showed moderate dysarthria during the assessment. This can however partly be explained by the fact that the Swedish clinical dysarthria assessment protocol (Hartelius, 2015; Hartelius & Svensson, 1990) includes tasks to capture all different sub-types of dysarthria. A hypokinetic dysarthria often leads to a low score even when moderate in its severity. No information on general disease severity was gathered for the participants with PD as a result of the participants having neurologist contacts at different clinics and it is not part of clinical practice everywhere to regularly and explicitly report for example Hoehn & Yahr staging scale (Hoehn and Yahr, 1967) ratings in the patient record.

4.7.1 Working with the VoxLog

The VoxLog was chosen for this thesis project as it is the only PVA that offers the ability to monitor noise level in addition to voice sound level, phonation ratio and fundamental frequency. The main voice parameter of interest for individuals with PD is the voice sound level, given that a decreased loudness is one of the most common symptoms in PD. As variations in noise level are expected to impact a speaker's voice sound level (Lombard,

1911), the ability to control for changes in noise level when studying voice sound level made the VoxLog the obvious choice of PVA for this project.

The microphone used in the VoxLog collar to register sound pressure level comes factory calibrated, eliminating the need for daily calibration as with for example the APM. The APM needs to be calibrated before each use as the voice sound level registered is estimated based on the activity in the accelerometer glued to the wearers throat. Variations in the calibration period can then introduce errors as different calibrations can impact the estimation of voice sound level. This is not a risk using the VoxLog with its combined accelerometer and microphone approach to voice registration. The fact that the accelerometer and microphone in the VoxLog are worn in a collar that is fitted around the neck, instead of an accelerometer glued to the neck, as with the APM, but this introduces another potential risk of measurement error. The microphone is situated at the neck approximately 10 cm from the mouth. The most common head position during conversation is with a somewhat neutral position facing straight ahead and small variations can be expected to not impact the values to a large extent. But during long periods of registration there will of course be many occasions where the wearer has spoken with her head turned or tilted which can alter the mouth-to-microphone distance. This is a source of error that must be taken into account when studying results from VoxLog registrations. It can however be expected that this variation to some extent would average outover a week-long registration period; one would expect situations both with a decreased and an increased mouth-to-microphone distance to occur during daily activities. Careful instructions were also given to all participants to always position the collar the same way each day to minimize the risk of varying mouth-to-microphone distances.

The mouth-to-microphone distance that results from the position of the VoxLog collar has to be taken into account when making comparisons of results to the more common 30 cm mouth-to-microphone distance. Voice sound level values can therefore seem quite high at a first glance. The data registered with the VoxLog is approximately 7.2 dB higher compared to a mouth-to-microphone distance of 30 cm (Wirebrand, 2012). Results have generally been shown in their original state in the studies in this thesis project to minimize the use of this approximation with the exception of study I. The approximation was used in study I to allow for an easier comparison with other studies as the aim of the study was to increase the knowledge of how PD impacts voice use, and not to experimentally assess the outcome of an intervention for example, as in study II, III and V.

Using the VoxLog has also introduced many technical challenges, especially broken devices and collars. This problem that was somewhat alleviated when Sonvox AB updated the design of the collars to a sturdier model. A recurring problem was also the cable between the VoxLog device and collar that tended to disconnect, leading to a loose or completely cut-off connection, often without the wearer noticing it immediately. These situations were intercepted, as all data was visually inspected for faulty registrations which were then removed from the analysis. It is however impossible to be sure that all errors were big or long enough to be clearly visible. Some smaller errors were probably missed and therefore stayed

forthe analysis. Registering voice use in daily life over long periods of time also leads to large amounts of data to process, all in all, data from 127 weeks of field registrations were analyzed in this project. With one data point being created for each 5 second time frame the resulting data set can be challenging to handle. The participants were asked to fill out a voice journal on paper during each day, intended to be used as a guide when analyzing the data. Initially, the goal was to use the voice journal to allow for more detailed analysis of voice use based on activity or perhaps different discreet communicative situations (number of participants during a conversation for example). Using a voice journal with handwritten notes is however not easy for individuals with PD, since micrographia and trouble writing by hand are common due to tremor and hypokinesia. Furthermore, not all participants remembered filling in the journal continuously during the whole registration period, so some data were missing in a few cases. The voice journal was therefore used to identify periods of voice use not representative of normal voice use. For example, one participant in study I attended choir practice and registrations during those periods were removed from the analysis as choir singing was interpreted as not representative of conversational speech. An automatic sound scene classifier, as describe in a PhD thesis by Peter Nordqvist (2004), or a digital voice journal, for example in the form of an app for a smartphone, could be a more feasible option to gather information in voice use for this population. Pre-defined choices could improve increased usability for the participants and make the grouping of activities easier during analysis. Such an app could also provide automated reminders to report into the voice journal, thus decreasing the risk for missing data.

4.7.2 The biofeedback capabilities of the VoxLog

When using the VoxLog's biofeedback function, there are some options that can be adjusted in the settings. These are the *threshold level*, at which voice sound level value the biofeedback will trigger if it goes above or below (for example 72 dB, can be set with a numerical number); the *activation time*, for what amount of time should the threshold level be passed before the biofeedback is triggered (for example 500 msec, can be set to predetermined values; 1 sec, 500 msec, 200 msec and 100 msec)*; rest time*, amount of time after a biofeedback activation that the biofeedback is deactivated so that it does not repeat the signal immediately (for example 10 seconds, can be set with a number). *Signal time*; length of the biofeedback activation (for example 1 second of vibration, can be set with a numerical number).

Changing the threshold level and the activation time will allow the most amount of control over how often the biofeedback will activate, i.e., the feedback frequency. This was used in study IV to test systematically what the resulting feedback frequency would be from six different predetermined settings. Even with these configurable settings, the ability to control the feedback manually is somewhat limited. The feedback can be delivered only in a direct manner, and not delayed, although the latter has have been found to promote retention in motor learning (Bislick et al., 2012; Maas et al., 2008). Neither can the device provide

summary feedback, used for example by Adams et al. (2002), where feedback from multiple trials is summarized after a period of time. The feedback settings are rigid and can be adjusted only when connecting the device to a computer with the accompanying software. Learners of different skill levels are helped by feedback in different ways, depending on where they are in their learning process (Guadagnoli & Lee, 2004). A more sophisticated feedback regime could provide direct feedback initially with a high-frequency, to help with acquisition of the skill and promote behavior change, and then adjust to a delayed, low-frequency feedback as training progresses. Such a modular approach could provide a more effective feedback schedule to help improve and consolidate a new skill.

There is also the question of whether a threshold level focusing on voice sound level is the most useful approach. The voice sound level required to make oneself heard in conversation depends on the level of the ambient noise. An adaptive biofeedback function with a threshold based on SOR instead of the voice sound level could be a more ecologically valid approach. The threshold level would then be adaptive based on noise level in the previous time frames during the continuous registration performed by the PVA, instead of a fixed threshold level as in for example the VoxLog.

5 CONCLUSIONS

Individuals with PD exhibit objectively measured limitations in communicative participation when studied in the form of phonation ratio. Individuals with PD used their voice 50-60% less, compared to matched healthy controls, during a week-long period of monitoring of voice use in daily life.

Monitoring voice use with a PVA can be a valuable complement to traditional voice assessment, because voice sound levels used during studio recordings in a controlled environment are not representative of voice sound levels used during monitoring in daily life, neither for individuals with PD nor for healthy controls.

Although limited in scope, the evaluation of treatment outcome regarding changes in voice sound level in daily life following LSVT LOUD® shows that changes previously reported during controlled recordings in a studio setting are reflected also in daily life.

When using a PVA for biofeedback purposes, the biofeedback should be carefully configured based on the individual's voice use during a baseline registration period. With the current capabilities of the VoxLog, a biofeedback threshold 3 dB below mean voice sound level and an activation time of 500 msec is recommended when the aim is to achieve a low-frequency feedback.

Results from this thesis indicates that providing continuous biofeedback regarding voice sound level in daily life with a PVA can help individuals with PD increase their voice sound level in relation to noise level, and thus to make themselves heard more easily.

6 CLINICAL IMPLICATIONS

Assessment of voice use and function in PD should include methods to study voice activity in a more ecologically valid and less controlled setting. This could be a valuable complement to the more controlled methods used today to further understand the challenges faced in daily life by patients with voice disorders. Objective information about voice use in daily life is also important when studying transfer and retention of skills acquired during voice treatment.

Providing direct biofeedback on voice use in daily life could be a valuable complement to traditional treatment of hypophonia in PD offered in a clinical setting, either as a method to help improve transfer and generalization of improved voice function following therapy, or as an option if traditional voice therapy such as for example LSVT LOUD® is not suitable for the individual. This could be applicable for younger individuals with PD who are still working and where it can be challenging to comply with a treatment period that entails sixteen visits to a voice clinic during a four-week period, or individuals with PD who might not have the energy to perform that many trips outside the home during such a short period of time. Promoting self-led training and exercise in the home can also empower the patient. The cost for the healthcare system is significantly reduced with fewer visits to the clinic. Reduced cognitive function may be a factor limiting possibilities to gain from biofeedback on voice sound level and should therefore be tested before including participants.

7 FUTURE DIRECTIONS

The use of portable voice accumulators to monitor voice use should preferably be accompanied by a voice journal to allow for a more detailed analysis and understanding of the material. An integrated, user-friendly, app could meet these needs, and also prompt the user to fill out the information regularly.

Further larger scale research is needed to determine the efficacy of using biofeedback regarding voice sound level to help treat hypophonia related to PD. Development of the capability to administer different biofeedback programs based on the user's skill level and progression during the training is needed to make the method more robust. An adaptable and modular feedback function that regulates the voice threshold level based on noise sound level during the speech and progressively increases the challenge for a more skilled individual would create ideal conditions to promote change.

In this project, the effects of biofeedback as a singular intervention method has been studied. It could be the case that biofeedback would be more effective as a complement to help patients with transfer and generalization after more traditional voice therapy. It would therefore be of great interest to see if the retention of treatment effects after LSVT LOUD®, for example, is increased by adding a period of biofeedback regarding voice sound level after the treatment period. The combination of both methods might be the ideal approach to help those individuals who struggle with applying their improved motor skills in their daily communication after treatment.

8 ACKNOWLEDGEMENTS

This work was supported by the Promobilia Foundation, NEURO Sweden, Capio Research Foundation, the Aina Börjesson Foundation for Speech Language Pathology Research and Treatment, the Swedish Parkinson Foundation and the Division of Speech and Language Pathology, Department of Clinical Science, Intervention and Technology, Karolinska Institutet.

This work would not have been possible without the support and contributions from a great number of people, the following in particular, whom I wish to thank:

All of the participants for their interest and kind cooperation.

Ellika Schalling, my main supervisor, who have guided me in every way possible throughout the years.

Maria Södersten, for her encouraging supervision and inspiration.

Sten Ternström, for his knowledgeable supervision and enlightening discussions.

Svante Granqvist, for invaluable help with MATLAB, saving me hours, and hours of work.

Elisabet Lundström, for all the support enabling me to combine research with clinical work.

Anette Lohmander, for all the encouragement and for creating a stimulating research environment.

Christina Hedestedt, for the never-ending and invaluable help with all the administration.

Frida Bulukin Wilén, for starting this path together with me, many years ago, and for being someone who makes any situation better, just by being you.

Jarrad van Stan, Robert Hillman and Daryush Mehta at the Voice Center in Boston for the most inspiring week of my life.

All current and past colleagues and fellow PhD students at the Division of Speech and Language Pathology for all the support and inspiring discussions.

All past and current colleagues at Karolinska University Hospital and Center for neurology for making work a place for laughter.

And more than anything, my family and friends. This would never have happened if not for you, Hanna. And my daughters, Greta and Brita who’s love makes every challenge easy to overcome.

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